includes other pharmaceutically active agents or drugs, such as chemotherapeutic agents, e.g., asparaginase, busulfan, carboplatin, cisplatin, daunorubicin, doxorubicin, fluorouracil, gemcitabine, hydroxyurea, methotrexate, paclitaxel, rituximab, vinblastine, and/or vincristine. The pharmaceutical composition in some embodiments contains the composition in amounts effective to treat or prevent the disease or condition, such as a therapeutically effective or prophylactically effective amount. Therapeutic or prophylactic efficacy in some embodiments is monitored by periodic assessment of treated subjects. The desired dosage can be delivered by a single bolus administration of the composition, by multiple bolus administrations of the composition, or by continuous infusion administration of the composition. In some embodiments, the pharmaceutical composition does not include a chemotherapeutic.

~~[0346]~~[0344] Formulations include those for oral, intravenous, intraperitoneal, subcutaneous, pulmonary, transdermal, intramuscular, intranasal, buccal, sublingual, or suppository administration. In some embodiments, the composition is administered parenterally. The term "parenteral," as used herein, includes intravenous, intramuscular, subcutaneous, rectal, vaginal, and intraperitoneal administration. In some embodiments, the composition is administered to the subject using peripheral systemic delivery by intravenous, intraperitoneal, or subcutaneous injection. Compositions in some embodiments are provided as sterile liquid preparations, e.g., isotonic aqueous solutions, suspensions, emulsions, dispersions, or viscous compositions, which may in some aspects be buffered to a selected pH. Liquid preparations are normally easier to prepare than gels, other viscous compositions, and solid compositions. Additionally, liquid compositions are somewhat more convenient to administer, especially by injection. Viscous compositions, on the other hand, can be formulated within the appropriate viscosity range to provide longer contact periods with specific tissues. Liquid or viscous compositions can comprise carriers, which can be a solvent or dispersing medium containing, for example, water, saline, phosphate buffered saline, polyol (for example, glycerol, propylene glycol, liquid polyethylene glycol) and suitable mixtures thereof.

~~[0347]~~[0345] Sterile injectable solutions can be prepared by incorporating the composition in a solvent, such as in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose, dextrose, or the like. The compositions can contain auxiliary substances such as wetting, dispersing, or emulsifying agents (e.g., methylcellulose), pH

buffering agents, gelling or viscosity enhancing additives, preservatives, flavoring agents, and/or colors, depending upon the route of administration and the preparation desired. Standard texts may in some aspects be consulted to prepare suitable preparations.

~~[0348]~~[0346] Various additives which enhance the stability and sterility of the compositions, including antimicrobial preservatives, antioxidants, chelating agents, and buffers, can be added. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, and sorbic acid. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

~~[0349]~~[0347] The formulations to be used for in vivo administration are generally sterile. Sterility may be readily accomplished, e.g., by filtration through sterile filtration membranes.

~~[0350]~~[0348] The embodiments provided for herein can be used for many purposes, since the a pseudotyped virus capable of fusing with a target cell can be used to deliver a gene or other heterologous sequence of interest.

ENUMERATED EMBODIMENTS

~~[0351]~~[0349] In some embodiments, the following embodiments are provided:

1. A VSV-G polypeptide comprising a mutation that corresponds to a mutation at position 182 of SEQ ID NO: 2.

2. The VSV-G polypeptide of embodiment 1, wherein the protein comprises an amino acid sequence of SEQ ID NO: 2 with a mutation at position 182 and has at least 70% identity to SEQ ID NO: 2.

3. The VSV-G polypeptide of embodiments 1 or 2, wherein the polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.

4. The VSV-G polypeptide of any one of embodiments 1-3, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 1 with a mutation at position 198 and at least

70% identity to SEQ ID NO: 2.

5. The VSV-G polypeptide of any one of embodiments 1-4, wherein the polypeptide comprises a mutation that corresponds to I182D or I182E as compared to a sequence of SEQ ID NO: 2.

6. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises an amino acid sequence at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence of SEQ ID NO: 4.

7. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises a sequence of SEQ ID NO: 4.

8. The VSV-polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises an amino acid sequence at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence of SEQ ID NO: 5.

9. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises a sequence of SEQ ID NO: 5.

10. The VSV-G polypeptide of any one of embodiments 1-9, further comprising a mutation in the VSV-G protein that corresponds to a mutation as described in US 2020/0216502, which is hereby incorporated by reference in its entirety.

11. The VSV-G polypeptide of any one of embodiments 1-10, further comprising a mutation in the VSV-G protein that corresponds to a position of 8, 10, 47, 209 and/or 354 as compared to SEQ ID NO: 2.

12. The VSV-G polypeptide of any one of embodiments 1-11, further comprising a mutation that corresponds to position 8 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except Y.

13. The VSV-G polypeptide of any one of embodiments 1-12, further comprising a mutation that corresponds to position 209 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except H.

14. The VSV-G polypeptide of any one of embodiments 1-13, further comprising a mutation that corresponds to position 47 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except K or R.

15. The VSV-G polypeptide of any one of embodiments 1-14, further comprising a mutation that corresponds to position 354 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except K or R.

16. The VSV-G polypeptide of any one of embodiments 1-15, further comprising a mutation that corresponds to position 10 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except Q or N.

17. The VSV-G polypeptide of any one of embodiments 1-16, wherein the protein comprises a substitution at position 47 or at position 354, or at both positions 47 and 354, wherein each position is, independently, substituted by A, G, F, Q, or N.

18. The VSV-G polypeptide of any one of embodiments 1-17, wherein the protein comprises a substitution at position 8, wherein the substitution is H8A, H8I, H8V, H8L, and the like.

19. The VSV-G polypeptide of any one of embodiments 1-18, wherein the protein comprises a substitution at position 47, wherein the substitution is K47Q or K47N.

20. The VSV-G polypeptide of any one of embodiments 1-19, wherein the protein comprises a substitution H8A and/or K47Q mutation.

21. The VSV-G polypeptide of any one of embodiments 1-20, wherein the protein comprises a substitution at position 10, such as Q10A, Q10R, or Q10K substitution.

22. The VSV-G polypeptide of any one of embodiments 1-21, further comprising a mutation that corresponds to a mutation at positions 214 and/or 352 of SEQ ID NO: 2.

23. The VSV-G polypeptide of embodiment 22, wherein the polypeptide comprises a T214N and/or T352A mutation.

24. A VSV-G polypeptide comprising a substitution at positions I182 and at least one of T214, and T352 of SEQ ID NO: 2.

25. The VSV-G polypeptide of embodiment 24, wherein the polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2.

26. The VSV-G polypeptide of embodiments 24 or 25, wherein the substitution at position 182 is I182D or I182E, the substitution at position 214 is T214N, and the substitution at position 352 is T352A.

27. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25.

28. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 22.

29. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 23.

30. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 24.

31. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 25.

32. A nucleic acid molecule encoding the VSV-G polypeptide of any one of embodiments 1-31.

33. A vector comprising the nucleic acid molecule of embodiment 32.

34. A plasmid comprising the nucleic acid molecule of embodiment 32.

35. A viral particle comprising the polypeptide of any one of embodiments 1-31.

36. The viral particle of embodiment 35, further comprising a targeting moiety.

37. The viral particle of embodiments 35 or 36, wherein the viral particle is a pseudotyped lentivirus.

38. The viral particle of any one of embodiments 35-37, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

39. The viral particle of embodiment 38, wherein the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof.

40. The viral particle of embodiments 38 or 39, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR").

41. The viral particle of any one of embodiments 35-40, wherein the targeting moiety binds to an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; "CD20+ cancer cell, CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

42. The viral particle of any one of embodiments 35-41, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2

(EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC), Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL1 lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule

(NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1).

43. The viral particle of any one of embodiments 35-42, wherein the targeting moiety is an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g., DARPIN), a VHH

domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof.

44. The viral particle of any one of embodiments 35-43, wherein the targeting moiety is attached to the viral surface through

an IgG Fc stalk;

an envelope glycoprotein G or H of a virus of the Paramyxoviridae family, such as a morbillivirus, such as Measles virus, or a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus;

a glycoprotein of a virus of the Rhabdoviridae family, such as a vesicular stomatitis New Jersey virus, a vesicular stomatitis Indiana virus, a vesicular stomatitis Alagoas virus, a vesicular stromatitis Maraba virus, a vesicular stomatitis Carajas virus, Parainfluenza virus, Spodoptera frugiperda rhabdovirus isolate Sf G, Drosophila obscura sigmavirus 10A, Wuhan insect virus 7, Perch virus, or Spring viremia of carp virus;

a glycoprotein of a virus of the Filoviridae family, such as Ebola virus; or

a glycoprotein of a virus of the Arenaviridae family, such as Machupo virus.

45. The viral particle of embodiment 44, wherein the stalk comprises a transmembrane domain, such as, but not limited to a CD8 or CD28 transmembrane domain.

46. A method of delivering a heterologous molecule to a target cell, the method comprising contacting the cell with a viral vector comprising:

a) the VSV-G protein of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

47. The method of embodiment 46, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+

haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

48. The method of embodiments 46 or 47, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle

stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(1- 4)bDGlcp(1-1)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL1 lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor

antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1) on the target cell.

49. A method of delivering a heterologous molecule to a target cell in a subject, the method comprising administering to the subject a viral vector comprising:

a) the VSV-G polypeptide of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

50. The method of embodiment 49, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T

cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

51. The method of embodiments 49 or 50, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19, CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6

located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-

3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1) on the target cell.

52. The method of any one of embodiments 46-51, wherein the heterologous molecule is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof, such as a chimeric antigen receptor ("CAR").

53. A method of treating cancer in a subject, the method comprising administering to the subject a viral vector comprising:

a) the VSV-G polypeptide of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

54. The method of embodiment 53, wherein the heterologous molecule is a chimeric antigen receptor.

55. The method of embodiments 53 or 54, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

56. The method of any one of embodiments 53-55, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3. A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123;

CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR);

Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein

72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1) on the target cell.

57. The method of any one of embodiments 53-56, wherein the cancer is a cancer as provided for herein, such as a T cell or B cell disorder.

58. The viral particle of any one of embodiments 35-45, wherein the targeting moiety binds to CD7.

59. The viral particle of embodiment 58, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

60. The viral particle of embodiment 59, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

61. The viral particle of embodiments 59 and 60, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set

forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

62. The viral particle of any one of embodiments 59-61, wherein the polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

63. The viral particle of any one of embodiments 59-62, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

64. The viral particle of any one of embodiments 59-63, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

65. The viral particle of any one of embodiments 59-64, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

66. The viral particle of any one of embodiments 59-65, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

67. The viral particle of any one of embodiments 59-66, wherein the heavy chain variable

region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker, which can be for example, a glycine/serine linker.

68. The viral particle of embodiment 67, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein n is independently 1-5.

69. The viral particle of any one of embodiments 58-68, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

70. The viral particle of any one of embodiments 58-68, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

71. The viral particle of any one of embodiments 35-45, wherein the targeting moiety binds to CD8.

72. The viral particle of embodiment 71, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

73. The viral particle of embodiment 72, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

74. The viral particle of embodiment 72 or 73, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

75. The viral particle of any one of embodiments 72-74, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

76. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

77. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

78. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

79. The viral particle of embodiment 71, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

80. The viral particle of any one of embodiments 72-79, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker.

81. The viral particle of embodiment 80, wherein the peptide linker is a glycine/serine linker.

82. The viral particle of embodiments 80 or 81, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

83. The viral particle of any one of embodiments 71-82, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

84. The viral particle of any one of embodiments 71-82, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

85. The method of any one of embodiments 46-57, wherein the targeting moiety that binds to the target cell binds to CD7.

86. The method of embodiment 85, wherein the targeting moiety comprises a polypeptide comprising: (i)a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

87. The method of embodiment 86, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

88. The method of embodiments 86 and 87, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

89. The method of any one of embodiments 86-88, wherein the polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth

in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

90. The method of any one of embodiments 86-89, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

91. The method of any one of embodiments 86-90, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

92. The method of any one of embodiments 86-91, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

93. The method of any one of embodiments 86-92, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

94. The method of any one of embodiments 86-93, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker, which can be for example, a glycine/serine linker.

95. The method of embodiment 94, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein n is independently 1-5.

96. The method of any one of embodiments 85-95, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ

ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

97. The method of any one of embodiments 85-95, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

98. The method of any one of embodiments 46-57, wherein the targeting moiety that binds to the target cell binds to CD8.

99. The method of embodiment 98, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

100. The method of embodiment 99, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

101. The method of embodiment 99 or 100, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID

NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

102. The method of any one of embodiments 99-101, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

103. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

104. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

105. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

106. The method of embodiment 98, wherein the CD8 targeting moiety comprises a polypeptide

comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

107. The method of any one of embodiments 99-106, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker.

108. The method of embodiment 107, wherein the peptide linker is a glycine/serine linker.

109. The method of embodiments 107 or 108, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

110. The method of any one of embodiments 98-109, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

111. The method of any one of embodiments 98-109, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

112. The viral particle of any one of embodiments 40-45 or 58-84, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 75.

113. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 75.

114. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding

domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 75.

115. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 75.

116. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 75.

117. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having the amino acid sequence of SEQ ID NO: 75.

118. The viral particle of any one of embodiments 40-45 or 58-84, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 76.

119. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 76.

120. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 76.

121. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 76.

122. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 76.

123. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having the amino acid sequence of SEQ ID NO: 76.

124. The method of any one of embodiments 46-57 or 85-111 wherein the heterologous molecule of interest is a chimeric antigen receptor (CAR), and wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 75.

125. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 75.

126. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 75.

127. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 75.

128. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 75.

129. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having the amino acid sequence of SEQ ID NO: 75.

130. The method of any one of embodiments 46-57 or 85-111 wherein the heterologous molecule of interest is a chimeric antigen receptor (CAR), and wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 76.

131. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 76.

132. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 76.

133. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 76.

134. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 76.

135. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having the amino acid sequence of SEQ ID NO: 76.

136. A viral particle comprising a targeting moiety that binds to CD7 or CD8, or a pharmaceutical composition comprising the same.

137. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

138. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36;

and HCDR3 as set forth in SEQ ID NO: 37.

139. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

140. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

141. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

141. The viral particle of embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

142. The viral particle embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy

chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

143. The viral particle embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

144. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

145. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

146. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety binds to CD8.

147. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the

amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

148. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

149. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

150. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

150. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

151. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

152. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

153. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

154. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

155. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

156. The viral particle of any one of embodiments 136-155, or a pharmaceutical composition

comprising the same, wherein the viral particle is a lentivirus derived viral particle.

157. The viral particle of any one of embodiments 136-156, or a pharmaceutical composition comprising the same, wherein the viral particle comprises a heterologous fusogenic protein, such as a glycoprotein from such as those provided for herein .

158. The viral particle of embodiment 157, or a pharmaceutical composition comprising the same, wherein the fusogenic protein is a VSV-G protein.

159. The viral particle of embodiment 158, or a pharmaceutical composition comprising the same, wherein the VSV-G protein is a mutant VSV-G protein.

160. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the mutant VSV-G protein abrogates binding to its natural co-receptor, such as LDL-R.

161. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the mutant VSV-G protein comprises a polypeptide of any one of embodiments 1-30.

162. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the viral particle comprises a nucleic acid molecule encoding a chimeric antigen receptor.

163. The viral particle of embodiment 162, or a pharmaceutical composition comprising the same, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD20.

164. The viral particle of embodiment 163, or a pharmaceutical composition comprising the same, wherein the antigen binding domain that binds to CD20 comprises a VH and VL as provided

for herein.

165. A method of delivering a heterologous molecule to a CD7+ or CD8+ target cell or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector comprising a targeting moiety that specifically binds to CD7 or CD8 on the target cell and a nucleic acid molecule encoding the heterologous molecule, wherein:

i) the targeting moiety that binds to CD7 comprises:

a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing;

a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37;

a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40;

a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in

SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40;

a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48;

a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48;

a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48;

a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51; or

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52; or

ii) the targeting moiety that binds to CD8 comprises:

a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3

sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing;

a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57;

a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60;

a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: wherein the

heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68;

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69; or

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

166. The method of embodiment 165, wherein the pseudotyped viral particle is a pseudotyped lentivirus derived viral particle.

167. The method of embodiments 165 or 166,wherein the pseudotyped viral particle comprises a heterologous fusogenic protein, such as a glycoprotein from those provided for herein .

168. The method of embodiment 167,wherein the fusogenic protein is a VSV-G protein.

169. The method of embodiment 168, wherein the VSV-G protein is a mutant VSV-G protein.

170. The method of embodiment 169, wherein the mutant VSV-G protein abrogates binding to its natural co-receptor, such as LDL-R.

171. The method of embodiment 169, wherein the mutant VSV-G protein comprises a polypeptide of any one of embodiments 1-30.

172. The method of any one of embodiments 165-171, wherein the heterologous nucleic acid molecule encodes for an siRNA, an shRNA, a non-coding RNA, a peptide, a polypeptide, a protein, a viral payload, a viral genome, a chimeric antigen receptor ("CAR") or a combination thereof.

173. The method of embodiment 172, wherein the heterologous nucleic acid molecule encodes

for a chimeric antigen receptor.

174. The method of embodiment 173, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD20.

175. The method of embodiment 174, wherein the antigen binding domain that binds to CD20 comprises a VH and VL as provided for herein and linked polypeptides comprising the same.

176. A cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein.

177. The cell of embodiment 176, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety that binds to CD7 or CD8.

178. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

179. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

180. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

181. The cell of embodiment 166, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

182. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

183. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a light chain and a heavy chain that comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

184. The cell of embodiment 183, wherein the light chain and the heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47;

and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

185. The cell of embodiment 183, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

186. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

187. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

188. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD8.

189. The cell of embodiment 188, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the

foregoing.

190. The cell of embodiment 188, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

191. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

192. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

193. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

194. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

195. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

196. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

197. The cell of embodiment 188, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

198. The cell of embodiment 188, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

199. The cells of any one of embodiments 176-198, wherein the heterologous nucleic acid molecule encoding the viral glycoprotein is a glycoprotein of any one of embodiments 1-30.

200. A cell comprising the nucleic acid molecule of embodiment 31, the vector of embodiment 32, or the plasmid of embodiment 33.

201. A method of making a viral particle comprising culturing the cell of any one of embodiments 176-198 under conditions sufficient to make the viral particle.

EXAMPLES

~~[0352]~~[0350] The following examples are illustrative, but not limiting, of the compounds,

compositions, particles, polypeptids, and methods described herein. Other suitable modifications and adaptations known to those skilled in the art are within the scope of the following embodiments.

Example 1: Mutation at position 182 of VSV-G abrogates LDL-R interaction, but retains fusing properties.

~~[0353]~~[0351] **Plasmids/Sequences.** All VSV-G plasmids were derived from pCMV-VSV-G Envelope Vector (Cell Bio Labs, catalog RV-110). Point mutations and combinations thereof were introduced using site directed mutagenesis (New England Biolabs). Individual mutations H8A and K47Q were previously shown to partially "blind" VSV-G, reducing its binding to LDL-R, the native cellular receptor for VSV (PMID: 29531262, DOI: 10.1038/s41467-018-03432-4). In this experiment, a single binder molecule consisting of a CD7-targeting scFv (clone MT701) fused to an IgG "stalk" bearing a CD28 transmembrane domain was used.

~~[0354]~~[0352] **Cells**. HEK293T cells were grown in DMEM with 10% FBS. SupT1 cells were maintained in RPMI media with 10% FBS. Human PBMCs were purchased from AllCells and cultured in X-Vivo 10 (Lonza) supplemented with 20ng/mL IL-2 (Peprotech). PBMCs were activated 48 hours prior to transduction using anti-CD3/CD28 Dynabeads (Cell Therapy Systems).

~~[0355]~~[0353] **Generation of lentiviral particles**. The recombinant lentiviral particles co-expressing VSV-G glycoprotein and binder molecules were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total of 5 plasmids were transfected: (1) plasmid expressing the VSV-G glycoprotein, (2) plasmid expressing the binder protein (3) plasmid expressing the lentiviral transfer genome encoding for eGFP, (4) plasmid expressing gag-pol, and (5) plasmid expressing rev. Transfected cell supernatant was harvested 48 hours later. Virus in the cell supernatant was concentrated by centrifugation through a sucrose cushion and resuspended in PBS. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

~~[0356]~~[0354] **Lentivirus transduction assay**. A series of 10-fold dilutions (in cell culture media) of the concentrated lentivirus was performed and used to infect SupT1 and activated human PBMCs. Media was replaced 6 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with a viability stain and an anti-CD7 antibody to detect CD7 positive cells (PeCy7 mouse-anti-human CD7, clone CD7-6B7, BD

Biosciences). Expression of eGFP was measured to calculate transduction efficiency.

~~[0357]~~[0355] **Structure-guided design of novel blinding mutations**. Using a published crystal structures of VSV-G bound to CR2 and CR3 of the LDL-R (pdb 50YL and 50Y9, respectively), we identified two putative positions in VSV-G with side chains oriented toward the binding interface on LDL-R (FIG. 1). Residue Q10 (SEQ ID NO: 2) appeared to form several interactions with residues in both CR2 and CR3. In CR3, this included interactions with a positively charged arginine residue. Thus, three substitutions were tested: Q10A to reduce side-chain interactions that potentially stabilize LDL-R binding and Q10R and Q10K to create electrostatic repulsion.

~~[0358]~~[0356] Residue I182 (SEQ ID NO: 2) appeared to contact several residues in both CR2 and CR3 as well. Three substitutions were tested: I182A to reduce side-chain interactions that potentially stabilize LDL-R binding and I182D and I182E to create electrostatic repulsion against the primary binding interfaces on LDL-R.

~~[0359]~~[0357] Addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. Titration of viral supernatants on the CD7+ T cell line SupT1 validated the structural predictions for residue I182. In the absence of any compensatory binder molecule, WT VSV-G reached titers of 3.0e8 while both I182D and I182E were ~3 orders of magnitude lower (Fig 2). Substitutions at residue I182 preserved fusogenicity, as titers were restored to 1e8 in the presence of a binder redirecting the virions to CD7.

~~[0360]~~[0358] The data is illustrated in FIG. 2, which shows that the addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. FIG.2A shows the titration of VSV-G constructs on SupT1 cells. Plotted is the percentage of SupT1 cells expressing GFP at each amount of viral input in terms of p24 antigen. Dashed lines/open circles indicate VSV-G constructs alone, solid lines/filled circles indicate the same construct with a CD7 targeting molecule expressed in trans. FIG. 2B illustrates Functional titer of each construct calculated from the titration in A, expressed as transducing units per mL of concentrated virus supernatant (TU/mL).

~~[0361]~~[0359] Thus these examples demonstrate that a mutation at position 182 is sufficient to abrogate the LDL-R interaction, but retain fusogenic properties when combining with a targeting moiety that binds to a target on the target cell.

Example 2: Serum Stable VSV-G Protein

~~[0362]~~[0360] WT VSV-G is reported to be sensitive to inactivation by naïve human serum, with inactivation ranging from minimal change to about 100-fold decrease depending on study parameters. Accordingly, it was assessed i) whether substitution at position I182 produced a variant VSV-G with similar sensitivity to serum and ii) whether incorporation of known serum stabilizing VSV-G mutations into the I182 substituted constructs had an effect on the serum stability of the constructs.

~~[0363]~~[0361] WT VSV-G, Serum Stable VSV-G (T214N, T352A), LDL-R de-targeted VSV-G (I182E), and LDL-R de-targeted serum stable VSV-G (I182E, T214N, T352A) were tested for their ability to infect SupT1 cells in the presence or absence of naïve serum or heat inactivated serum (HI) (FIG. 4). As expected WT VSV-G had a dramatic decrease in percent infectivity when administered in the presence of serum with a mild rescue of infectivity if serum was heat inactivated (HI) (FIG. 4, columns 1-3). The inclusion of the CD7 targeting moiety on an IgG1 Fc stalk (WT) did not rescue the serum inactivation (FIG. 4, columns 4-6). The VSV-G constructs harboring the T214N and T352A mutations showed a similar reduction in infectivity in the presence of serum with no distinction between naïve or HI serum (FIG. 4, columns 7-9). However, the inclusion of the targeting moiety was able to partially rescue the inactivation in either serum condition (FIG. 4, columns 10-12). Surprisingly, the LDL-R de-targeted VSV-G (I182E) showed no reduction in infectivity percentage in the presence of either serum condition (FIG. 4, columns 13-15), but rather showed increased infectivity in the presence of naïve serum as compared to serum free or HI serum conditions. Further inclusion of the known serum stable mutations into VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in the presence of serum as compared to serum free conditions (FIG. 4, columns 16-18). Further, the I182E, T214N, T352A construct also demonstrates increased infectivity in the presence of HI serum (FIG. 4, column 18), which indicates that the triple mutant construct has a higher degree of serum stability than the other constructs examined.

~~[0364]~~[0362] To further characterize the effect of including serum stabilizing mutations in the viral constructs of the present application, WT VSV-G, VSV-G (I182E), and VSV-G (I182E, T230N, T352A) were assessed at a lower dose of vector (FIG. 5). In agreement with the previous assessment, WT VSV-G showed decreased infectivity in serum as compared to no-serum

conditions (FIG. 5, columns 1 and 2). However, heat inactivation (HI) of serum did appear to have a rescuing effect on WT VSV-G infectivity (FIG. 5, column 3). In further agreement with the previous assessment, VSV-G (I182E) demonstrated enhanced infectivity in the presence of serum as compared to no serum conditions (FIG. 5, columns 4 and 5). The presence of HI serum also resulted in an increased infectivity compared to no serum, with a smaller effect than naïve serum (FIG. 5, column 6). VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in serum and HI serum conditions as compared to no serum conditions (FIG. 5, columns 7-9), in agreement with the previous assessment. Further, when compared to the respective no serum condition, VSV-G (I182E, T230N, T352A) results in a greater percent increased infectivity compared to VSV-G (I182E), suggesting that inclusion of all three mutations results in greater serum stability than just I182E alone.

~~[0365]~~[0363] Thus, these examples demonstrate that i) the LDL-R detargeting mutation I182E affords an unexpected level of protection against the serum inactivation observed for WT VSV-G, ii) the LDL-R detargeting mutation I182E does not abrogate the serum stabilizing effect of the T230N + T352A mutations, and iii) the combined mutation construct VSV-G (I182E, T230N, T352A) appears to have a greater serum stabilizing effect than either I182E alone or T230N + T352A alone. Thus, VSV-G (I182E, T230N, T352A) is able to ablate native tropism without alternating fusogenicity and additionally demonstrates a more stable profile and is not neutralized in serum.

Example 3: CD7 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.

~~[0366]~~[0364] Generation of Plasmids and Sequences.

~~[0367]~~[0365] The amino acid sequence including CDRs of the CD7 binder was determined via mass spectrometry (Rapid Novor). CD7 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD7 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD7 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

~~[0368]~~[0366] Generation of Engineered Lentiviral Particles.

~~[0369]~~[0367] The recombinant lentiviral particles expressing the CD7 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the IgG stalk or a plasmid expressing the CD7 binder on a Nipah-G protein, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev.In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the Nipah-G protein, (2) plasmid expressing Nipah-F protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA)

~~[0370]~~[0368] CD7 binders attach to both human and non-human primate PBMCs, leading to CD7+ cell transduction.

~~[0371]~~[0369] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with an anti-CD7 antibody to detect CD7 positive cells (PE-Cy7 mouse-anti-human CD7, clone MT-701, Biolegend) as well as GFP expression. Cell viability was also determined. CD7 binders attached to Paramyxoviridae glycoproteins, such as Nipah-G (FIG. 6A-D and FIG. 7A-D) or with Rhabdoviridae glycoproteins, such as VSV-G (FIG. 6I-L and FIG. 7I-L) successfully transduced human PBMCs (FIG. 6A-L) or NHP PBMCs (FIG. 7A-L) compared to the binder alone (FIG. 6E-H and FIG. 7E-H) which shows no transduction. When CD7 with an IgG stalk was tested, the binder alone (top row) again did not transduce human (FIG. 6M) or NHP PBMCs (FIG. 7M) but when administered with detargeted VSV-G, transduction was seen in both human (FIG. 6M, bottom panel) and NHP PBMCs (FIG. 7M, bottom panel). GFP transduction experiments were repeated as described above for detargeted VSV-G pseudotyped lentiviral constructs with CD7 binders. Results of the repeat experiments were in agreement with the data

of FIGS 6 and 7 and are provided in Table 1 below.

TABLE 1

	WT VSVG	Detartgeted VSVG	CD7 Binder (SEQ ID NO. 51)	CD7 Binder (SEQ ID NO. 52)	CD8 Binder (SEQ ID NO. 69)	CD7 Binder (SEQ ID NO. 70)
Human PBMC Transduction (% positive)	52.76	0.00798	19.32	21.55	4.09	3.17
NHP PBMC Transduction (% positive)	48.4	0.026	2.61	5.64	1.8	0.76

~~[0372]~~[0370] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD7 and target viral particles to cells expressing CD7 to transduce the cells expressing CD7.

Example 4: CD8 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.

~~[0373]~~[0371] Generation of Plasmids and Sequences.

~~[0374]~~[0372] The amino acid sequence including CDRs of the CD8 binder was determined via mass spectrometry (Rapid Novor). CD8 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD8 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD8 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

~~[0375]~~[0373] Generation of Engineered Lentiviral Particles.

~~[0376]~~[0374] The recombinant lentiviral particles expressing the CD8 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD8 binder with the IgG stalk, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. In some embodiments, the lentiviral genome expressing eGFP was

replaced with a CAR molecule. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

~~[0377]~~[0375] CD8 binders attach to both human and non-human primate PBMCs, leading to CD8+ cell transduction.

~~[0378]~~[0376] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 6 after transduction. Cells were stained with an anti-CD8 antibody to detect CD8 positive cells (BV421 mouse-anti-human CD8, clone RPA-T8, Biolegend) as well as GFP or CAR20 expression. Cell viability was also determined. CD8 binders with detargeted VSV-G successfully transduced human PBMCs (FIG. 8A) or NHP PBMCs (FIG. 8B) with GFP (FIG. 8A-8B, top row) and CAR20 (FIG. 8A-8B, bottom row). GFP transduction experiments were repeated as described above for detargeted VSV-G pseudotyped lentiviral constructs with CD8 binders. Results of the repeat experiments were in agreement with the data of FIG 8 and are provided in Table 1 above.

~~[0379]~~[0377] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD8 and target viral particles to cells expressing CD8 to transduce the cells expressing CD8.

~~[0380]~~[0378] **Example 5: Binder construct affects transgene expression.**

~~[0381]~~[0379] Concentrated lentivirus was used to transduce SupT1 cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry. Cells were stained with an anti-CD8 antibody to detect CD8 positive cells or an anti-CD7 antibody to detect CD7 positive cells as well as GFP or CAR20 expression.

~~[0382]~~[0380] Lentiviral constructs utilizing CD7 or CD8 binders as provided for herein exhibited comparable GFP transduction (FIG. 9A). Binder orientation (VH-VL vs VL-VH) had minimal effect on transgene expression. WT VSV-G was used as a positive control, and detargeted VSV-G was used as a negative control. With respect to a CD20-CAR transgene, lentiviral

constructs utilizing CD7 binders as provided for herein provided superior transgene transduction as compared to lentiviral constructs utilizing CD8 binders (FIG. 9B). As with the GFP transgene, binder orientation had minimal effect on transgene expression. Lentiviral constructs utilizing CD7 or CD8 binders both demonstrated transgene expression levels near the level of WT VSV-G when greater amounts of virus were utilized.

~~[0383]~~[0381] These examples and embodiments demonstrate that the CD7 and CD8 binders of the present disclosure can be incorporated into a lentiviral particle to direct successful transgene expression in a target cell. Further, these examples and embodiments demonstrate that different binders result in differential transgene expression, and that both the identity of the binder and the identity of the transgene are important variable in the efficacy of the viral particle.

~~[0384]~~[0382] **Example 6: VSV-G* pseudotyped lentiviruses harboring CD7 binder transduce PBMCs.**

~~[0385]~~[0383] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. A CD7 binder construct was utilized in the present example. The CD7 binder was as provided for herein. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 10A) compared to the binder alone (FIG. 10B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 10C).

~~[0386]~~[0384] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses are able to successfully transduce a variety of human and non-human primate PMBCs.

~~[0387]~~[0385] Example 7: VSV-G* pseudotyped lentiviruses harboring a CD7 binder exhibit minimal off target transduction.

~~[0388]~~[0386] The off target transduction of B-cells via VSV-G* pseudotyped lentiviral

constructs utilizing CD7 binders as provided for herein was assessed in several B-cell populations. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. B-cells cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect the various B-cell populations. A CD7 binder construct was utilized in the present example. The CD7 binder was as provided for herein. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 5 after transduction to determine GFP transduction. As a control, SupT1 cells were also infected with the same lentiviral constructs. None of the B-cell populations assessed demonstrated any significant level of GFP expression (FIG. 11A).

~~[0389]~~[0387] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner. VSV-G* pseudotyped lentiviruses utilizing the CD7 binder still exhibited minimal off target transduction of B-cells in all cell populations tested (FIG. 11B). The percent of CAR-T2A-GFP positive cells only exceeded 1% in line DB at the highest lentiviral concentrations utilized.

~~[0390]~~[0388] These examples and embodiments demonstrate that the i) VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure have low off target transduction of B-cells and ii) delivery of a CAR20 transgene instead of a GFP transgene does not significantly increase off target transduction in B-cells.

Example 8: VSV-G* pseudotyped lentiviruses with CD20-CAR transgene payload kills CD20 positive lymphoma cells *in vitro*

~~[0391]~~[0389] The ability of VSV-G* pseudotyped lentiviral constructs with a CD20-CAR transgene to kill CD20 positive lymphoma cells *in vitro* was assessed. The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Human PBMCs were transduced with a lentiviral construct carrying a CD20-CAR (CAR20) transgene. The CAR20 transgenes comprised antigen binding

domains of SEQ ID NO: 75 or SEQ ID NO: 76. CD20 positive lymphoma cells were then added to the CAR20 cells at a given effector to target ratio (E:T). All lentiviral constructs tested produced a dose dependent killing of CAR20 positive lymphoma cells (FIG 12)

~~[0392]~~[0390] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure not only transduce the appropriate target cells as demonstrated by the previous examples, but also produce robust and dose dependent killing of CD20 positive lymphoma cells *in vivo*.

Example 9: VSV-G* pseudotyped lentiviruses deplete B-cells and eliminate established tumors in mice.

~~[0393]~~[0391] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was assessed. The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Mice were injected with lentiviral particles expressing a GFP transgene, or a CD20-CAR transgene. The mice utilized were huCD34 NSG mice which have circulating human T and B cells. Mice receiving lentiviral constructs expressing GFP saw no loss of CD20 (FIG. 13A) or CD19 (FIG. 13B) B cells. Mice receiving the CD20-CAR transgene saw a dramatic and sustained loss of B cells over three weeks as exhibited by a dramatic loss of both CD20 positive B cells (FIG. 13A) and CD19 positive B cells (FIG. 13B).

~~[0394]~~[0392] To further characterize the *in vivo* efficacy of the viral particles, the ability of VSV-G* pseudotyped lentiviral constructs to prevent tumor formation was assessed. Mice were injected with viral particles expressing a GFP transgene or a CD20-CAR transgene on protocol Day 1. On Day 9, mice were infused with Raji tumor cells and tumor progression was monitored. The experimental protocol illustrated in FIG. 14A. Mice receiving no treatment or lentiviral constructs expressing GFP demonstrated progressive tumor development and spread as determined by IVIS imaging. In contrast, mice receiving lentiviral constructs expressing the CD20-CAR transgene demonstrated no tumor development after Raji cell infusion (FIG. 14B).

~~[0395]~~[0393] The ability of the viral particles to affect established tumors *in vivo* was also assessed. Mice were infused with Raji tumor cells on protocol Day 0. Mice were humanized via

human PBMC engraftment on protocol Day 5, and mice were either not injected with viral particles (control) or injected with viral particles expressing a CD20-CAR transgene on protocol Day 6. Tumor progression was monitored through protocol Day 30. The experimental protocol is illustrated in FIG. 15A. Control and virus treated mice demonstrated comparable tumor load on Day 5 (prior to virus administration), Day 7, and Day 8 as determined by IVIS imaging, indicating that Raji tumors were established in both groups. At Day 12, control mice continued to exhibit increased tumor load, whereas virus treated mice exhibited a dramatic decrease in tumor load. The decreased tumor load was sustained throughout the duration of the experiment (FIG. 15B).

~~[0396]~~[0394] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviral constructs of the present disclosure are able to properly target B-cells *in vivo*, prevent tumor formation *in vivo*, and eliminate established tumors *in vivo*.

Example 10: VSV-G* pseudotyped lentiviruses deplete B-cells in non-human primates.

~~[0397]~~[0395] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was also assessed in non-human primates (Macaques). The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Macaques were injected with lentiviral particles on protocol Day 0 and their CD20+ cells were monitored. Injection of the lentiviral particles results in B-cell depletion in 6/6 Macaques tested.

~~[0398]~~[0396] This specification contains numerous citations to patents, patent applications, and publications. Each is hereby incorporated by reference for all purposes.

~~[0399]~~[0397] The specification also makes reference to various sequences, such as those provided herein and below.

VSV-G Indiana Full length WT:
MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHA
SKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDE
YTGEWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETG
GKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIR
AGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIG

PNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWK
SSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 1)

VSV-G Indiana Ectodomain WT:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 2)

VSV-G Indiana ectodomain I182A:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLASMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 3)

VSV-G Indiana ectodomain I182D:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLDSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 4)

VSV-G Indiana ectodomain I182E:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLESMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 5)

VSV-G Indiana ectodomain H8A + K47Q:
KFTIVFPANQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 6)

VSV-G Indiana ectodomain Q10A:
KFTIVFPHNAKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY

MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 7)

VSV-G Indiana ectodomain Q10R:
KFTIVFPHNSKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 8)

VSV-G Indiana ectodomain Q10K:
KFTIVFPHNNKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 9)

VSV-G New Jersey Full length WT:
MLSYLIFALVVSPILGKIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHS
ALWMTTCDFRWYGPKYITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAEAHIVTVTPHSVKVDE
YTGEWIDPHFIGGRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVST
EGICKMPFCRKPGYKLKNDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTW
SKIEAGEPITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYLRVELESPVIPRMEGKVAGTRIVRQLWDQWFPFGE
VEIGPNGVLKTKQGYKFPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGDTGVSKNPVELVE
GWFSGWRSSIMGVLAVIIGFVILIFLIPLIGVLSSLFRQKRRPIYKSDVEMAHFR (SEQ ID NO: 10)

VSV-G New Jersey ectodomain WT:
KIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHSALWMTTCDFRWYGPKY
ITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAEAHIVTVTPHSVKVDEYTGEWIDPHFIGGRCK
GQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVSTEGICKMPFCRKPGYKL
KNDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTWSKIEAGEPITPVDLSY
LGPKNPGAGPVFTIINGSLHYFMSKYLRVELESPVIPRMEGKVAGTRIVRQLWDQWFPFGEVEIGPNGVLKTKQGYK
FPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGDTGVSKNPVELVEGWFSGWRSSIMGVLAV
IIGFVILIFLIRLIGVLSSLFRQKRRPIYKSDVEMAHFR (SEQ ID NO: 11)

VSV-G Marraba Full length WT:
MLRLFLFCFLALGAHSKFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLIGVSLHVKIPKSHKAIQADGWMCHA
AKWVTTCDFRWYGPKYITHSIHSMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAEVVVVQATPHHVLVDE
YTGEWIDSQLVGGKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTSLGKPNTGFRSNHFAYESG
EKACRMQYCTQWGIRLPSGVWFELVDKDLFQAAKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIR
AKLPVSPVDLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTMSGTTTERELWNDWYPYEDVEIG
PNGVLKTPTGFKFPLYMIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSSWK
STLASFFLIIGLGVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 12)

VSV-G Marraba ectodomain WT:
KFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVSLHVKIPKSHKAIQADGWMCHAAKWVTTCDFRWYGPKY

ITHSIHSMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAEVVVVQATPHHVLVDEYTGEWIDSQLVGGKCS
KEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTSLGKPNTGFRSNHFAYESGEKACRMQYCTQWGIRL
PSGVWFELVDKDLFQAAKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAKLPVSPVDLSYLAPK
NPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTMSGTTTERELWNDWYPYEDVEIGPNGVLKTPTGFKFPLY
MIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSSWKSTLASFFLIIGLGVAL
IFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 13)

VSV-G Carajas Full length WT:
MKMKMVIAGLILCIGILPAIGKITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLIDIGLRLRAPKSFKGISADG
WMCHAARWITTCDFRWYGPKYITHSIHSFRPSNDQCKEAIRLTNEGNWINPGFPPQSCGYASVTDSESVVVTVTKHQ
VLVDEYSGSWIDSQFPGGSCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPNSGIRSNYF
PYESLKDVCQMDFCKRKGFKLPSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSL
CQATWSKIQNKEALTPIDISYLGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGFVSGTSTSRVLWDQW
FPYGENSIGPNGLLKTASGYKYPLFMVGTGVLDADIHKLGEATVIEHPHAKEAQKVVDDSEVIFFGDTGVSKNPVEV
VEGWFSGWRSSLMSIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRRA (SEQ ID NO: 14)

VSV-G Carajas ectodomain WT:
KITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLIDIGLRLRAPKSFKGISADGWMCHAARWITTCDFRWYGPKY
ITHSIHSFRPSNDQCKEAIRLTNEGNWINPGFPPQSCGYASVTDSESVVVTVTKHQVLVDEYSGSWIDSQFPGGSCT
SPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPNSGIRSNYFPYESLKDVCQMDFCKRKGFKL
PSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSLCQATWSKIQNKEALTPIDISY
LGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGFVSGTSTSRVLWDQWFPYGENSIGPNGLLKTASGYK
YPLFMVGTGVLDADIHKLGEATVIEHPHAKEAQKVVDDSEVIFFGDTGVSKNPVEVVEGWFSGWRSSLMSIFGIILL
IVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRRA (SEQ ID NO: 15)

VSV-G Alagoa Full length WT:
MTPAFILCMLLAGSSWAKFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDLLGVNIRAKMPKVHKAIKADGWMCH
AAKWVTTCDYRWYGPQYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHSVMID
EYSGDWLDSQFPTGRCTGSTCETIHNSTLWYADYQVTGLCDSALVSTEVTFYSEDGLMTSIGRQNTGYRSNYFPYEK
GAAACRMKYCTHEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSLCQETWSKV
HSGLPISPVDLGYIAPKNPGAGPAFTIVNGTLKYFDTRYLRIDIEGPVLKKMTGKVSGTPTKRELWTEWFPYDDVEI
GPNGVLKTPEGYKFPLYMIGHGLLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKNPVEVIEGWFSNW
RSSVMAIVFAILLLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 16)

VSV-G Alagoa ectodomain WT:
KFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDLLGVNIRAKMPKVHKAIKADGWMCHAAKWVTTCDYRWYGPQY
ITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHSVMIDEYSGDWLDSQFPTGRCT
GSTCETIHNSTLWYADYQVTGLCDSALVSTEVTFYSEDGLMTSIGRQNTGYRSNYFPYEKGAAACRMKYCTHEGIRL
PSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSLCQETWSKVHSGLPISPVDLGYIAPK
NPGAGPAFTIVNGTLKYFDTRYLRIDIEGPVLKKMTGKVSGTPTKRELWTEWFPYDDVEIGPNGVLKTPEGYKFPLY
MIGHGLLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKNPVEVIEGWFSNWRSSVMAIVFAILLLVIT
VLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 17)

VSV-G Cocal Full length WT:
MNFLLLTFIVLPLCSHAKFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQADGWMCH
AAKWITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDSVAVVVQATPHHVLVD
EYTGEWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPNTGYRSNYFAYEK
GDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKI
RSKQPVSPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEI
GPNGILKTPTGYKFPLFMIGHGMLDSDLHKTSQAEVFEHPHLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSW

KSTVVTFFFAIGVFILLYVVARIVIAVPYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 18)

VSV-G Cocal ectodomain WT:
KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQADGWMCHAAKWITTCDFRWYGPKY
ITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDSVAVVVQATPHHVLVDEYTGEWIDSQFPNGKCE
TEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPNTGYRSNYFAYEKGDKVCKMNYCKHAGVRL
PSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEIGPNGILKTPTGYKFPLF
MIGHGMLDSDLHKTSQAEVFEHPHLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSWKSTVVTFFFAIGVFILL
YVVARIVIAVPYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 19)

VSV-G Morreton Full length WT:
MLVLYLLLSLLALGAQCKFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWHNGLIGTSLQVKMPKSHKAIQADGWMCH
AAKWVTTCDFRWYGPKYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAEAVIVKATPHQVLVD
EYTGEWVDSQFPTGKCNKDICPTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYEN
GDKACRMQYCKHWGVRLPSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKI
RAHLPISPVDLSYLSPKNPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEI
GPNGVLKTATGYKFPLYMIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGW
KSTIASFFFIIGLVIGLYLVLRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 20)

VSV-G Morreton ectodomain WT:
KFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWHNGLIGTSLQVKMPKSHKAIQADGWMCHAAKWVTTCDFRWYGPKY
VTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAEAVIVKATPHQVLVDEYTGEWVDSQFPTGKCN
KDICPTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYENGDKACRMQYCKHWGVRL
PSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAHLPISPVDLSYLSPK
NPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEIGPNGVLKTATGYKFPLY
MIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGWKSTIASFFFIIGLVIGL
YLVLRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 21)

Fc IgG1 (Accession No. P01857)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)

Fc IgG2 (Accession No. AAN76043)
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFN
WYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPP
SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

Fc IgG4 (Accession No. AAB59394)
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
KTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF
NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLP
PSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH
EALHNHYTQKSLSLSLGK (SEQ ID NO: 28)

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 63/289,888 filed 15 December 2021, and U.S. Provisional Application Ser. No. 63/289,977 filed 15 December 2021, and U.S. Provisional Application Ser. No. 63/266,044 filed 27 December 2021, and U.S. Provisional Application Ser. No. 63/267,039 filed 21 January 2022, each of which is hereby incorporated by reference in their entirety.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on 28 November 2022, is named "148165.001401_SL.xml" and is 86.3 kilobytes in size.

BACKGROUND

[0003] Vesicular stomatitis virus (VSV) is an enveloped, negative-strand RNA virus that belongs to the Vesiculovirus genus of the Rhabdovirus family. It is an arbovirus which can infect insects, cattle, horses and pigs. VSV genome encodes five structural proteins among which include a single transmembrane glycoprotein (G). The glycoprotein is a classic type I membrane glycoprotein with an amino-terminal signal peptide, an ectodomain of about 450 amino acids, a single alpha helical transmembrane segment and a small intraviral carboxy-terminal domain. The signal peptide is cleaved in the lumen of the endoplasmic reticulum and the native glycoprotein consists in the ectodomain, the transmembrane domain and the intraviral domain.

[0004] G plays a critical role during the initial steps of virus infection (Molecular and Cellular Aspects of Rhabdovirus Entry. Viruses 4, 117-139.), which is hereby incorporated by reference in its entirety. First, it is responsible for virus attachment to specific receptors. After binding, virions enter the cell by a clathrin-mediated endocytic pathway. In the acidic environment of the endocytic vesicle, G triggers the fusion between the viral and endosomal membranes, which releases the genome in the cytosol for the subsequent steps of infection. Fusion is catalyzed by a

low-pH-induced large structural transition from a pre-toward a post-fusion conformation which are both trimeric (Roche, S., Bressanelli, S., Rey, F. A., and Gaudin, Y. (2006). Crystal structure of the low-pH form of the vesicular stomatitis virus glycoprotein G. Science 313, 187-191. Roche, S., Rey, F. A., Gaudin, Y., and Bressanelli, S. (2007). Structure of the prefusion form of the vesicular stomatitis virus glycoprotein g. Science 315, 843-848), each of which is hereby incorporated by reference in its entirety).

[0005] The polypeptide chain of G ectodomain folds into three distinct domains which are the fusion domain (FD), the pleckstrin homology domain (PHD), and the trimerization domain (TrD). During the structural transition, the FD, the PHD and the TrD retain their tertiary structure. Nevertheless, they undergo large rearrangements in their relative orientation due to secondary changes in hinge segments (S1 to S5) which refold during the low-pH induced conformational change (Roche et al., 2006; Roche et al., 2007).

[0006] It has been shown that low-density lipoprotein receptor (LDL-R) and other members of this receptor family serve as VSV receptors (Finkelshtein, D., Werman, A., Novick, D., Barak, S., and Rubinstein, M. (2013). LDL receptor and its family members serve as the cellular receptors for vesicular stomatitis virus. Proceedings of the National Academy of Sciences of the United States of America 110, 7306-7311, which is hereby incorporated by reference in its entirety). VSV-G can be used for pseudotyping other viruses and VSV-G-pseudotyped lentiviruses (VSV-G-LVs) exhibit the same broad tropism as VSV. However, this broad tropism can inhibit the selective targeting of specific cell types. Therefore, there is a need, for modified (mutated or mutant) VSV-G proteins that can be used to pseudotype viruses that abrogate its binding to the LDL receptor. The present embodiments, fulfill these needs as well as others.

[0007] The human CD7 molecule is a cell surface glycoprotein with a molecular weight of approximately 40 kDa belonging to the immunoglobulin superfamily. The CD7 molecule is mainly expressed on the surface of most thymocytes, more than 85% of the surface of peripheral blood T lymphocytes and the surface of natural killer cells. The embodiments disclosed herein provide for polypeptide and antibodies against CD7, compositions comprising the same, and uses thereof.

[0008] CD8 (cluster of differentiation 8) is a transmembrane glycoprotein which is a specific marker for a subclass of T-cells (which includes cytotoxic T-cells). Without wishing to be bound to a particular theory, CD8 assembles as either a heterodimer of the CD8 alpha and CD8

beta subunits or a CD8 alpha homodimer. The assembled dimeric CD8 complex acts as a co-receptor together with the T cell receptor (TCR) to recognize antigen presentation by MHC class I cells. CD8 plays a role in the development of T-cells and activation of mature T-cells. Changes in T-cell localization can reflect the progression of an immune response and can occur over time. The embodiments disclosed herein provide for polypeptide and antibodies against CD8, compositions comprising the same, and uses thereof.

BRIEF SUMMARY

[0009] In some embodiments, a VSV-G polypeptide is provided. In some embodiments, the VSV-G polypeptide comprises a mutation at position 182 of SEQ ID NO: 2. In some embodiments, the polypeptide comprises an I182E or I182D mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 4. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 5.

[0010] In some embodiments, the VSV-G polypeptide further comprises a mutation in the VSV-G protein that corresponds to a position of 8, 10, 47, 209, and/or 354 as compared to SEQ ID NO: 2. In some embodiments, the VSV-G polypeptide comprises a H8A and/or a K47Q substitution. In some embodiments, the VSV-G polypeptide comprises a substitution at position 10 as compared to SEQ ID NO: 2. In some embodiments, the substitution at position 10 is Q10A, Q10R, or Q10K.

[0011] In some embodiments, a VSV-G polypeptide is provided. In some embodiments, the VSV-G polypeptide comprises a substitution at position I182 and at least one of T214, and T352 of SEQ ID NO: 2. In some embodiments, the VSV-G polypeptide comprises a substitution at position I182, T214, and T352 of SEQ ID NO: 2. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 22. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 23. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 24. In some embodiments, the VSV-G polypeptide comprises the sequence of SEQ ID NO: 25.

[0012] In some embodiments, a nucleic acid molecule is provided. In some embodiments, the nucleic acid molecule encodes for the VSV-G polypeptide as provided for herein.

[0013] In some embodiments, a vector is provided comprising a nucleic acid molecule as

provided for herein.

[0014] In some embodiments, a plasmid is provided comprising a nucleic acid molecule as provided for herein.

[0015] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a VSV-G polypeptide as provided for herein. In some embodiments, the viral particle further comprises a targeting moiety. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding for a heterologous molecule of interest.

[0016] In some embodiments, a method of delivering a heterologous molecule of interest to a target cell is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

[0017] In some embodiments, a method of delivering a heterologous molecule of interest to a target cell in a subject is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

[0018] In some embodiments, a method of treating cancer in a subject is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

[0019] In some embodiments, the targeting moiety of the viral particle binds to CD7. In some embodiments, the targeting moiety comprises a polypeptide comprising a heavy chain CDR1 having the amino acid sequence of SEQ ID NO: 35, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 36, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 37, a light chain CDR1 having the amino acid sequence of SEQ ID NO: 38, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 39, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 40. In some embodiments, the targeting moiety comprises a

polypeptide comprising a heavy chain variable region having the amino acid sequence of SEQ ID NO: 47 and a light chain variable region having the amino acid sequence of SEQ ID NO: 48.

[0020] In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51. In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising the sequence of SEQ ID NO: 51.

[0021] In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, at least 95% sequence identity to SEQ ID NO: 52, at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52. In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising the sequence of SEQ ID NO: 52.

[0022] In some embodiments, the targeting moiety of the viral particle binds to CD8. In some embodiments, the targeting moiety comprises a polypeptide comprising a heavy chain CDR1 having the amino acid sequence of SEQ ID NO: 55, a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 56, a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 57, a light chain CDR1 having the amino acid sequence of SEQ ID NO: 58, a light chain CDR2 having the amino acid sequence of SEQ ID NO: 59, a light chain CDR3 having the amino acid sequence of SEQ ID NO: 60. In some embodiments, the targeting moiety comprises a polypeptide comprising a heavy chain variable region having the amino acid sequence of SEQ ID NO: 67 and a light chain variable region having the amino acid sequence of SEQ ID NO: 68.

[0023] In some embodiments, the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69. In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising the sequence of SEQ ID NO: 69.

[0024] In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, at least 95% sequence identity to SEQ ID NO: 70, at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70. In some embodiments, the targeting moiety that

binds to CD7 comprises a polypeptide comprising the sequence of SEQ ID NO: 70.

[0025] In some embodiments, a method of delivering a heterologous molecule of interest to a target cell is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety as provided for herein that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments the targeting moiety binds to CD7. In some embodiments, the targeting moiety binds to CB8. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

[0026] In some embodiments, a method of delivering a heterologous molecule of interest to a target cell in a subject is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety as provided for herein that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments the targeting moiety binds to CD7. In some embodiments, the targeting moiety binds to CB8. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

[0027] In some embodiments, a method of treating cancer in a subject is provided. In some embodiments, the method comprises contacting the cell with a viral vector comprising a VSV-G protein as provided for herein, a targeting moiety as provided for herein that binds to the target cell, and a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments the targeting moiety binds to CD7. In some embodiments, the targeting moiety binds to CB8. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor.

BRIEF DESCRIPTION OF FIGURES

[0028] FIG. 1A and FIG. 1B illustrate crystal structures of VSV-G bound to LDL-R. FIG. 1A illustrates the crystal structure of VSV-G bound to CR3 of the LDL-R. FIG. 1B illustrates the crystal structure of VSV-G bound to CR2 of the LDL-R.

[0029] FIG. 2A and FIG. 2B illustrate the effect of adding negatively charged amino acids to the VSV-G:LDL-R binding interface on native tropism and fusogenicity. FIG.2A illustrates the titration of VSV-G constructs on SupT1 cells. FIG. 2B illustrates functional titer of each construct calculated from the titration in FIG. 2A.

[0030] FIG. 3 illustrates an alignment of the ectodomains of different VSV-G proteins from different strains.

[0031] FIG. 4 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0032] FIG. 5 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0033] FIG. 6A-L show flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0034] FIG. 6M shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0035] FIG. 7A-L shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0036] FIG. 7M shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0037] FIG. 8A shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0038] FIG. 8B shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0039] FIG. 9A and FIG. 9B illustrate GFP or CAR transduction of SupT1 cells utilizing VSV-G pseudotyped lentiviral particles harboring CD7 or CD8 binders as provided for herein. FIG. 9A illustrates GFP transduction. FIG. 9B illustrates CAR transduction.

[0040] FIG. 10A illustrates the ability of VSV-G* pseudotyped lentiviral particles harboring a CD7 binder to transduce SupT1 cells as well as human and non-human primate PBMCs. FIG. 10B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 10C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration. VSV-G* denotes VSV-G polypeptide comprising I182E, T214N, T352A, which corresponds to a mature polypeptide of SEQ ID NO: 23 or SEQ ID NO: 25 (with I196E, T230N and T368A mutations (with leader sequence and adjusted numbering).

[0041] FIG. 11A and FIG. 11B illustrate the off target transduction of VSV-G* pseudotyped lentiviral particles harboring a CD7 binder in a panel of B-cell cell lines as compared

to control SupT1 cells. FIG. 11A illustrates the data for GFP transduction. FIG. 11B illustrates the data for CAR20-T2A-GFP transduction. VSV-G* denotes a VSV-G polypeptide comprising I182E, T214N, and T352A mutations as provided for herein.

[0042] FIG. 12A and FIG. 12B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to kill Duadi lymphoma cells (FIG. 12A) or Raji lymphoma cells (FIG. 12B). CAR20 constructs utilized antigen binding domains comprising rituximab, or CD20AB1 SEQ ID NOs 75 or 76 as provided for herein.

[0043] FIG. 13A and FIG. 13B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to deplete B-cells *in vivo* in huCD34 NSG mice. B-cells were detected via assessment for CD20 (FIG. 13A) or CD19 (FIG. 13B).

[0044] FIG. 14A and FIG. 14B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to prevent tumor formation *in vivo*. FIG. 14A depicts the experimental design. FIG. 14B illustrates that mice receiving i.v. lentiviral particles as provided for herein prior to Raji tumor infusion had significantly lower tumor burden than mice receiving control (GFP) vector or untreated mice. Tumor burden measured via IVIS imaging.

[0045] FIG. 15A and FIG. 15B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to eliminate estabilished Raji tumors *in vivo*. FIG. 15A depicts the experimental design. FIG. 15B illustrates that mice receiving i.v. lentiviral particles as provided for herein after 6 days after Raji tumor infusion had their tumor burdens diminished below the limit of detection. Tumor burden measured via IVIS imaging.

DETAILED DESCRIPTION

[0046] Provided for herein are mutant VSV-G proteins that can be used, for example, to pseudotype a virus, such as a lentivirus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of a vesicular stomatitis New Jersey virus strain, a vesicular stomatitis Indiana virus strain, a vesicular stomatitis Alagoas virus strain, a vesicular

stromatitis Maraba virus strain, or a vesicular stomatitis Carajas virus strain.

[0047] The pseudotyped viruses comprising the mutant VSV-G proteins can be used in conjunction with a targeting moiety to facilitate the fusion of the pseudotyped virus with a specific cell or tissue based on the expression of the target on the cell or the tissue.

[0048] Unless defined otherwise, all technical and scientific terms have the same meaning as is commonly understood by one of ordinary skill in the art to which the embodiments disclosed belongs.

[0049] As used herein, the terms "a" or "an" means that "at least one" or "one or more" unless the context clearly indicates otherwise.

[0050] As used herein, the term "about" means that the numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical limitation is used, unless indicated otherwise by the context, "about" means the numerical value can vary by ±10% and remain within the scope of the disclosed embodiments. Additionally, where a phrase recites "about x to y," the term "about" modifies both x and y and can be used interchangeably with the phrase "about x to about y" unless context dictates differently.

[0051] "Activation," as used herein in reference to a T cell, refers to the state of a T cell that has been sufficiently stimulated to induce detectable cellular proliferation. Activation can also be associated with induced cytokine production, and detectable effector functions. The term "activated T cells" refers to, among other things, T cells that are undergoing cell division.

[0052] As used herein, to "alleviate" a disease means reducing the severity of one or more symptoms of the disease.

[0053] The term "antigen" as used herein is defined as a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically-competent cells, or both. The skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. The term "antigen" can also refer to a molecule that an antibody or antibody-like molecule can bind to or is recognized by the antibody or antibody-like molecule.

[0054] The term "antibody molecule," "antibody" or antigen binding domain, as that term is used herein, refers to a polypeptide, e.g., an immunoglobulin chain or fragment thereof,

comprising at least one functional immunoglobulin variable domain sequence. An antibody molecule encompasses antibodies (e.g., full-length antibodies) and antibody fragments. In some embodiments, an antibody molecule comprises an antigen binding or functional fragment of a full-length antibody, or a full-length immunoglobulin chain. For example, a full-length antibody is an immunoglobulin (Ig) molecule (e.g., an IgG antibody) that is naturally occurring or formed by normal immunoglobulin gene fragment recombinatorial processes. In embodiments, an antibody molecule refers to an immunologically active, antigen binding portion of an immunoglobulin molecule, such as an antibody fragment. An antibody fragment, e.g., functional fragment, comprises a portion of an antibody, e.g., Fab, Fab′, F(ab′)2, F(ab)2, variable fragment (Fv), domain antibody (dAb), or single chain variable fragment (scFv). A functional antibody fragment binds to the same antigen as that recognized by the intact (e.g., full-length) antibody. The terms "antibody fragment" or "functional fragment" also include isolated fragments consisting of the variable regions, such as the "Fv" fragments consisting of the variable regions of the heavy and light chains or recombinant single chain polypeptide molecules in which light and heavy variable regions are connected by a peptide linker ("scFv proteins"). In some embodiments, an antibody fragment does not include portions of antibodies without antigen binding activity, such as Fc fragments or single amino acid residues. Exemplary antibody molecules include full-length antibodies and antibody fragments, e.g., dAb (domain antibody), single chain, Fab, Fab', and F(ab')2 fragments, and single chain variable fragments (scFvs).

[0055] The term "antibody molecule" also encompasses whole or antigen binding fragments of domain, or single domain, antibodies, which can also be referred to as "sdAb" or "VHH." Domain antibodies comprise either VH or VL that can act as stand-alone, antibody fragments. Additionally, domain antibodies include heavy-chain-only antibodies (HCAbs). Domain antibodies also include a CH2 domain of an IgG as the base scaffold into which CDR loops are grafted. It can also be generally defined as a polypeptide or protein comprising an amino acid sequence that is comprised of four framework regions interrupted by three complementarity determining regions. This is represented as FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4. sdAbs can be produced in camelids such as llamas, but can also be synthetically generated using techniques that are well known in the art. The numbering of the amino acid residues of a sdAb or polypeptide is according to the general numbering for VH domains given by Kabat et al. ("Sequence of proteins

of immunological interest," US Public Health Services, NIH Bethesda, MD, Publication No. 91, which is hereby incorporated by reference). According to this numbering, FR1 of a sdAb comprises the amino acid residues at positions 1-30, CDR1 of a sdAb comprises the amino acid residues at positions 31-36, FR2 of a sdAb comprises the amino acids at positions 36-49, CDR2 of a sdAb comprises the amino acid residues at positions 50-65, FR3 of a sdAb comprises the amino acid residues at positions 66-94, CDR3 of a sdAb comprises the amino acid residues at positions 95-102, and FR4 of a sdAb comprises the amino acid residues at positions 103-113. Domain antibodies are also described in WO2004041862 and WO2016065323, each of which is hereby incorporated by reference. The domain antibodies can be a targeting moiety as described herein.

[0056] As used herein, unless otherwise indicated, "antibody fragment" or "antigen binding fragment" refers to antigen binding fragments of antibodies, *i.e.* antibody fragments that retain the ability to bind specifically to the antigen bound by the full-length antibody, *e.g.* fragments that retain one or more CDR regions. Examples of antibody binding fragments include, but are not limited to, Fab, Fab', $F(ab')_2$, and Fv fragments; diabodies; linear antibodies; single-chain antibody molecules, *e.g.*, sc-Fv; nanobodies (single domain antibody) and multispecific antibodies formed from antibody fragments.

[0057] A "Fab fragment" is comprised of one light chain and the C_H1 and variable regions of one heavy chain. The heavy chain of a Fab molecule cannot form a disulfide bond with another heavy chain molecule.

[0058] An "Fc" region contains two heavy chain fragments comprising the C_H2 and C_H3 domains of an antibody. The two heavy chain fragments are held together by two or more disulfide bonds and by hydrophobic interactions of the C_H3 domains.

[0059] A "Fab' fragment" contains one light chain and a portion or fragment of one heavy chain that contains the V_H domain and the C_H1 domain and also the region between the C_H1 and C_H2 domains, such that an interchain disulfide bond can be formed between the two heavy chains of two Fab' fragments to form a $F(ab')_2$ molecule.

[0060] A "$F(ab')_2$ fragment" contains two light chains and two heavy chains containing a portion of the constant region between the C_H1 and C_H2 domains, such that an interchain disulfide bond is formed between the two heavy chains. A $F(ab')_2$ fragment thus is composed of two Fab'

fragments that are held together by a disulfide bond between the two heavy chains.

[0061] The "Fv region" comprises the variable regions from both the heavy and light chains, but lacks the constant regions.

[0062] The term "single-chain Fv" or "scFv" antibody refers to antibody fragments comprising the V_H and V_L domains of an antibody, wherein these domains are present in a single polypeptide chain. Generally, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the scFv to form the desired structure for antigen binding. For a review of scFv, see Pluckthun (1994) THE PHARMACOLOGY OF MONOCLONAL ANTIBODIES, vol. 113, Rosenburg and Moore eds. Springer-Verlag, New York, pp. 269-315. See also, International Patent Application Publication No. WO 88/01649 and U.S. Pat. Nos. 4,946, 778 and 5,260,203.

[0063] Antibody molecules can be monospecific (e.g., monovalent or bivalent), bispecific (e.g., bivalent, trivalent, tetravalent, pentavalent, or hexavalent), trispecific (e.g., trivalent, tetravalent, pentavalent, or hexavalent), or with higher orders of specificity (e.g, tetraspecific) and/or higher orders of valency beyond hexavalency. An antibody molecule can comprise a functional fragment of a light chain variable region and a functional fragment of a heavy chain variable region, or heavy and light chains may be fused together into a single polypeptide.

[0064] Furthermore, antigens can be derived from recombinant or genomic DNA. A skilled artisan will understand that any DNA, which comprises a nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response therefore encodes an "antigen" as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full length nucleotide sequence of a gene. Moreover, a skilled artisan will understand that an antigen need not be encoded by a "gene" at all. It is readily apparent that an antigen can be generated synthesized or can be derived from a biological sample. Such a biological sample can include, but is not limited to a tissue sample, a tumor sample, a cell or a biological fluid.

[0065] In certain embodiments, monoclonal antibodies herein also include camelized single domain antibodies. *See, e.g.,* Muyldermans *et al.* (2001) *Trends Biochem. Sci.* 26:230; Reichmann *et al.* (1999) *J. Immunol. Methods* 231:25; WO 94/04678; WO 94/25591; U.S. Pat. No. 6,005,079). In one embodiment, the present invention provides single domain antibodies

comprising two V_H domains with modifications such that single domain antibodies are formed.

[0066] As used herein, the term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy chain variable domain (V_H) connected to a light chain variable domain (V_L) in the same polypeptide chain (V_H-V_L or V_L-V_H). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, *e.g.*, EP 404,097; WO 93/11161; and Holliger *et al.* (1993) *Proc. Natl. Acad. Sci. USA* 90: 6444-6448. For a review of engineered antibody variants generally see Holliger and Hudson (2005) *Nat. Biotechnol.* 23:1126-1136.

[0067] "Isolated antibody" refers to the purification status of a binding compound and in such context means the molecule is substantially free of other biological molecules such as nucleic acids, proteins, lipids, carbohydrates, or other material such as cellular debris and growth media. Generally, the term "isolated" is not intended to refer to a complete absence of such material or to an absence of water, buffers, or salts, unless they are present in amounts that substantially interfere with experimental or therapeutic use of the binding compound as described herein.

[0068] The term "monoclonal antibody", as used herein, refers to population of substantially homogeneous antibodies, *i.e.*, the antibody molecules comprising the population are identical in amino acid sequence except for possible naturally occurring mutations and/or post-translational modifications that may be present in minor amounts. In contrast, conventional (polyclonal) antibody preparations typically include a multitude of different antibodies having different amino acid sequences in their variable domains, particularly their CDRs, that are often specific for different epitopes. The modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the present invention may be made by the hybridoma method first described by Kohler *et al.* (1975) *Nature* 256: 495, or may be made by recombinant DNA methods (*see, e.g.*, U.S. Pat. No. 4,816,567). The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson *et al.* (1991) *Nature* 352: 624-628 and Marks *et al.* (1991) *J. Mol. Biol.* 222: 581-597, for example. *See also* Presta (2005) *J. Allergy Clin. Immunol.* 116:731.

[0069] As used herein, the term "humanized antibody" refers to forms of antibodies that contain sequences from both human and non-human (*e.g.*, murine, rat) antibodies. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the hypervariable loops correspond to those of a non-human immunoglobulin, and all or substantially all of the framework (FR) regions are those of a human immunoglobulin sequence. The humanized antibody may optionally comprise at least a portion of a human immunoglobulin constant region (Fc).

[0070] The term "fully human antibody" refers to an antibody that comprises human immunoglobulin protein sequences only. A fully human antibody may contain murine carbohydrate chains if produced in a mouse, in a mouse cell, or in a hybridoma derived from a mouse cell. Similarly, "mouse antibody" refers to an antibody that comprises mouse immunoglobulin sequences only. Alternatively, a fully human antibody may contain rat carbohydrate chains if produced in a rat, in a rat cell, or in a hybridoma derived from a rat cell. Similarly, "rat antibody" refers to an antibody that comprises rat immunoglobulin sequences only.

[0071] In some embodiments, the basic antibody structural unit comprises a tetramer. Each tetramer includes two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of the heavy chain may define a constant region primarily responsible for effector function. Typically, human light chains are classified as kappa and lambda light chains. Furthermore, human heavy chains are typically classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 10 more amino acids. See generally, *Fundamental Immunology* Ch. 7 (Paul, W., ed., 2nd ed. Raven Press, N.Y. (1989).

[0072] The variable regions of each light/heavy chain pair form the antibody binding site. Thus, in general, an intact antibody has two binding sites. However, in bifunctional or bispecific antibodies, the two binding sites are, in general, not the same.

[0073] Typically, the variable domains of both the heavy and light chains comprise three

hypervariable regions, also called complementarity determining regions (CDRs), located within relatively conserved framework regions (FR). The CDRs are usually aligned by the framework regions, enabling binding to a specific epitope. In general, from N-terminal to C-terminal, both light and heavy chains variable domains comprise FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain is, generally, in accordance with the definitions of *Sequences of Proteins of Immunological Interest*, Kabat, *et al.*; National Institutes of Health, Bethesda, Md. ; 5th ed.; NIH Publ. No. 91-3242 (1991); Kabat (1978) Adv. Prot. Chem. 32:1-75; Kabat, *et al.*, (1977) J. Biol. Chem. 252:6609-6616; Chothia, *et al.*, (1987) J Mol. Biol. 196:901-917 or Chothia, *et al.*, (1989) Nature 342:878-883.

[0074] As used herein, the term "hypervariable region" refers to the amino acid residues of an antibody that are responsible for antigen-binding. The hypervariable region comprises amino acid residues from a "complementarity determining region" or "CDR" (*i.e.* residues 24-34 (CDRL1), 50-56 (CDRL2) and 89-97 (CDRL3) in the light chain variable domain and residues 31-35 (CDRH1), 50-65 (CDRH2) and 95-102 (CDRH3) in the heavy chain variable domain; Kabat *et al.* (1991) Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md.) and/or those residues from a "hypervariable loop" (*i.e.* residues 26-32 (CDRL1), 50-52 (CDRL2) and 91-96 (CDRL3) in the light chain variable domain and 26-32 (CDRH1), 53-55 (CDRH2) and 96-101 (CDRH3) in the heavy chain variable domain; Chothia and Lesk (1987) *J. Mol. Biol.* 196: 901-917). The CDRs can also be referenced according to the IMGT system for the identification of CDRs, which is described in Lefranc MP. Unique database numbering system for immunogenetic analysis. Immunol Today (1997) 18:509. As used herein, the term "framework" or "FR" residues refers to those variable domain residues other than the hypervariable region residues defined herein as CDR residues. CDRs provide the majority of contact residues for the binding of the antibody to the antigen or epitope. CDRs of interest can be derived from donor antibody variable heavy and light chain sequences, and include analogs of the naturally occurring CDRs, which analogs also share or retain the same antigen binding specificity and/or neutralizing ability as the donor antibody from which they were derived.

[0075] As used herein, "specific binding" or "immunospecific binding" or "binds immunospecifically" refer to antibody binding to a predetermined antigen at a much higher affinity than for another antigen(s). In some embodiments, the antibody binds the predetermined antigen

with a dissociation constant (K_D) of 10^{-7} M or less, and such K_D is at least two-fold less than its K_D for binding to a non-specific antigen (*e.g.*, BSA, casein, or another non-specific polypeptide).

[0076] Methods for determining mAb specificity and affinity by competitive inhibition can be found in Harlow, et al., Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1988), Colligan et al., eds., Current Protocols in Immunology, Greene Publishing Assoc. and Wiley Interscience, N.Y., (1992, 1993), and Muller, Meth. Enzymol. 92:589 601 (1983), which references are entirely incorporated herein by reference.

[0077] As used herein, the term "individual" or "subject," or "patient" used interchangeably, means any animal, including mammals, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, such as humans. In some embodiments, the subject is a human. A subject that is "in need thereof" refers to a subject that has been identified as requiring treatment for the condition that is to be treated and is treated with the specific intent of treating such condition. The conditions can be, for example, any of the conditions described herein.

[0078] As used herein, the terms "comprising" (and any form of comprising, such as "comprise", "comprises", and "comprised"), "having" (and any form of having, such as "have" and "has"), "including" (and any form of including, such as "includes" and "include"), or "containing" (and any form of containing, such as "contains" and "contain"), are inclusive or open-ended and do not exclude additional, unrecited elements or method steps. Any step or composition that uses the transitional phrase of "comprise" or "comprising" can also be said to describe the same with the transitional phase of "consisting of" or "consists."

[0079] As used herein, the term "contacting" means bringing together of two elements in an in vitro system or an in vivo system. For example, "contacting" virus or vector described herein with an individual or patient or cell includes the administration of the virus to an individual or patient, such as a human, as well as, for example, introducing a compound into a sample containing a cellular or purified preparation containing the cell.

[0080] As used herein, the term "fused" or "linked" when used in reference to a protein having different domains or heterologous sequences means that the protein domains are part of the same peptide chain that are connected to one another with either peptide bonds or other covalent bonding. The domains or section can be linked or fused directly to one another or another domain

or peptide sequence can be between the two domains or sequences and such sequences would still be considered to be fused or linked to one another. In some embodiments, the various domains or proteins provided for herein are linked or fused directly to one another or a linker sequences, such as the glycine/serine sequences described herein link the two domains together.

[0081] A "disease" is a state of health of an animal wherein the animal cannot maintain homeostasis, and wherein if the disease is not ameliorated then the animal's health continues to deteriorate. In contrast, a "disorder" in an animal is a state of health in which the animal is able to maintain homeostasis, but in which the animal's state of health is less favorable than it would be in the absence of the disorder. Left untreated, a disorder does not necessarily cause a further decrease in the animal's state of health.

[0082] "Effective amount" or "therapeutically effective amount" are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result or provides a therapeutic or prophylactic benefit. Such results may include, but are not limited to an amount that when administered to a mammal, causes a detectable level of immune cell activation compared to the immune cell activation detected in the absence of the composition. The immune response can be readily assessed by a plethora of art-recognized methods. The skilled artisan would understand that the amount of the composition administered herein varies and can be readily determined based on a number of factors such as the disease or condition being treated, the age and health and physical condition of the mammal being treated, the severity of the disease, the particular compound being administered, and the like.

[0083] "Encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (i.e., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that

gene or cDNA.

[0084] "Expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., Sendai viruses, lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[0085] As used herein, the phrase "ex vivo" in reference to a cell being transduced, transfected or transformed ex vivo, refers to a cell being transduced, transfected or transformed outside of the subject, that is with the cells being removed from the subject before such cells are transduced, transfected or transformed.

[0086] "Identity" as used herein refers to the subunit sequence identity between two polymeric molecules such as between two nucleic acid or amino acid molecules, such as, between two polynucleotide or polypeptide molecules. When two amino acid sequences have the same residues at the same positions; e.g., if a position in each of two polypeptide molecules is occupied by an Arginine, then they are identical at that position. The identity or extent to which two amino acid or two nucleic acid sequences have the same residues at the same positions in an alignment is often expressed as a percentage. The identity between two amino acid or two nucleic acid sequences is a direct function of the number of matching or identical positions; e.g., if half of the positions in two sequences are identical, the two sequences are 50% identical; if 90% of the positions (e.g., 9 of 10), are matched or identical, the two amino acids sequences are 90% identical.

[0087] By "substantially identical" is meant a polypeptide or nucleic acid molecule exhibiting at least 50% identity to a reference amino acid sequence (for example, any one of the amino acid sequences described herein) or nucleic acid sequence (for example, any one of the nucleic acid sequences described herein). In some embodiments, such a sequence is at least 60%, 80% or 85%, or 90%, 95% or even 99% identical at the amino acid level or nucleic acid to the sequence used for comparison. Other percentages of identity in reference to specific sequences are described herein.

[0088] Sequence identity can be measured/determined using sequence analysis software

(for example, Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, Wis. 53705, BLAST, BESTFIT, GAP, or PILEUP/PRETTYBOX programs). Such software matches identical or similar sequences by assigning degrees of homology to various substitutions, deletions, and/or other modifications. Conservative substitutions typically include substitutions within the following groups: glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid, asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. In an exemplary approach to determining the degree of identity, a BLAST program may be used, with a probability score between e3 and e100 indicating a closely related sequence. In some embodiments, sequence identity is determined by using BLAST with the default settings.

[0089] To the extent embodiments provided for herein, includes composition comprising various proteins, these proteins may, in some instances, comprise amino acid sequences that have sequence identity to the amino acid sequences disclosed herein. Therefore, in certain embodiments, depending on the particular sequence, the degree of sequence identity is preferably greater than 50% (e.g. 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more) to the SEQ ID NOs disclosed herein. In addition to these percentages, other percentages of identity are provided for herein. Identity between polypeptides can be determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affine gap search with parameters gap open penalty – 12 and gap extension penalty = 1.

[0090] These proteins may, compared to the disclosed proteins, include one or more (e.g. 1, 2, 3,4, 5, 6, 7, 8, 9, 10, etc.) conservative amino acid replacements i.e. replacements of one amino acid with another which has a related side chain. Genetically-encoded amino acids are generally divided into four families: (1) acidic i.e. aspartate, glutamate; (2) basic i.e. lysine, arginine, histidine; (3) non polar i.e. alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar i.e. glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In general, Substitution of single amino acids within these families does not have a major effect on the biological activity. The proteins may have one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) single amino acid deletions relative to the disclosed protein sequences.

The proteins may also include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) insertions (e.g. each of 1, 2, 3, 4 or 5 amino acids) relative to the disclosed protein sequences.

[0091] As used herein, the phrase "in vivo" in reference to a cell being transduced, transfected or transformed in vivo, refers to a cell being transduced, transfected or transformed in the subject without the cells being removed from the subject before such cells are transduced, transfected or transformed.

[0092] "Isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

[0093] A "lentivirus" as used herein refers to a genus of the Retroviridae family that is able to infect non-dividing cells. Non-limiting examples of lentiviruses are HIV, SIV, and FIV. Vectors or viral-like particles derived from lentiviruses can be used to transduce cells and deliver genes or other molecules and have them expressed in a cell either in vitro (ex-vivo) or in vivo.

[0094] By the term "modified" as used herein, is meant a changed state or structure of a molecule or cell as provided herein. Molecules may be modified in many ways, including chemically, structurally, and functionally, such as mutations, substitutions, insertions, or deletions (e.g. internal deletions truncations). Cells may be modified through the introduction of nucleic acids or the expression of heterologous proteins.

[0095] By the term "modulating," as used herein, is meant mediating an increase or decrease in the level of a response in a subject compared with the level of a response in the subject in the absence of a treatment or compound, and/or compared with the level of a response in an otherwise identical but untreated subject. The term encompasses perturbing and/or affecting a native signal or response thereby mediating a beneficial therapeutic response in a subject, such as, a human.

[0096] As used herein, the following abbreviations for the commonly occurring nucleic acid bases are used: "A" refers to adenosine, "C" refers to cytosine, "G" refers to guanosine, "T" refers to thymidine, and "U" refers to uridine.

[0097] Unless otherwise specified, a "nucleotide sequence encoding an amino acid

sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or an RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

[0098] The "Nipah virus" (NiV) is member of the family Paramyxoviridae, genus Henipavirus. Nipah virus is an enveloped virus with negative-stranded polarity and a non-segmented RNA genome consisting of helical nucleocapsids. Two strains of Nipah virus include, but are not limited to, the Malaysian (MY) and the Bangladesh (BD) strains.

[0099] The term "oligonucleotide" typically refers to short polynucleotides. It will be understood that when a nucleotide sequence is represented by a DNA sequence (i.e., A, T, C, G), this also provides the corresponding RNA sequence (i.e., A, U, C, G) in which "U" replaces "T."

[0100] "Parenteral" administration of a composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, or infusion techniques.

[0101] The term "polynucleotide" as used herein is defined as a chain of nucleotides. Furthermore, nucleic acids are polymers of nucleotides. Thus, the terms "nucleic acids" and "polynucleotides" as used herein are interchangeable. As used herein polynucleotides include, but are not limited to, all nucleic acid sequences which are obtained by any methods available in the art, including, without limitation, recombinant methods, i.e., the cloning of nucleic acid sequences from a recombinant library or a cell genome, using cloning technology and PCR, and the like, and by synthetic means.

[0102] As used herein, the terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of a plurality of amino acid residues covalently linked by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. The polypeptides include natural peptides, recombinant peptides, synthetic peptides, or a combination thereof.

[0103] The term "pseudotyped" or "pseudotyped viral particle", as used herein, refers to a

viral particle bearing glycoproteins derived from other viruses having envelopes or a viral vector encoding envelope glycoproteins from a virus that is different from the parental virus. The host range of the vector particles can thus be expanded or altered depending on the type of cell surface receptor used by the glycoprotein. For example, a virus can be pseudotyped with a VSV-G mutant protein as provided for herein or other virus glycoproteins, such as those provided for herein.

[0104] By the term "specifically binds," as used herein with respect to an antibody, is meant an antibody which recognizes a specific antigen, but does not substantially recognize or bind other molecules in a sample. For example, an antibody that specifically binds to an antigen from one species may also bind to that antigen from one or more species. But, such cross-species reactivity does not itself alter the classification of an antibody as specific. In another example, an antibody that specifically binds to an antigen may also bind to different allelic forms of the antigen. However, such cross reactivity does not itself alter the classification of an antibody as specific. In some instances, the terms "specific binding" or "specifically binding," can be used in reference to the interaction of an antibody, a protein, or a peptide with a second chemical species, to mean that the interaction is dependent upon the presence of a particular structure (e.g., an antigenic determinant or epitope) on the chemical species; for example, an antibody recognizes and binds to a specific protein structure rather than to proteins generally. If an antibody is specific for epitope "A", the presence of a molecule containing epitope A (or free, unlabeled A), in a reaction containing labeled "A" and the antibody, will reduce the amount of labeled A bound to the antibody. In some embodiments, the targeting moieties described herein that can be used to target the viral particles comprising the mutant VSV-G protein can specifically bind to their target.

[0105] The term "subject" includes living organisms, including those in which an immune response can be elicited (e.g., mammals). A "subject" or "patient," as used therein, may be a human or non-human mammal. Non-human mammals include, for example, livestock and pets, such as ovine, bovine, porcine, canine, non-human primates, feline and murine mammals. In some embodiments, the subject is human.

[0106] The term "therapeutic" as used herein means a treatment and/or prophylaxis. A therapeutic effect is obtained by suppression, remission, or eradication of a disease state.

[0107] The term "transfected" or "transformed" or "transduced" as used herein refers to a process by which exogenous nucleic acid is transferred or introduced into a cell. A "transfected"

or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny. In some embodiments, the transfection, transformation, or transduction is performed or occurs in vivo.

[0108] To "treat" a disease as the term is used herein, means to reduce the frequency or severity of at least one sign or symptom of a disease or disorder experienced by a subject. As used herein, "inhibit" or "treat" or "treatment" also includes a postponement of development of the symptoms associated with a disorder and/or a reduction in the severity of the symptoms of such disorder. The terms further include ameliorating existing uncontrolled or unwanted symptoms, preventing additional symptoms, and ameliorating or preventing the underlying causes of such symptoms. Thus, the terms denote that a beneficial result has been conferred on a vertebrate subject with a disorder, disease or symptom, or with the potential to develop such a disorder, disease or symptom.

[0109] A "vector" is a composition of matter which comprises an isolated nucleic acid encoding a protein or a peptide. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, plasmids, DNA, and RNA. Examples of viral vectors include, but are not limited to, Sendai viral vectors, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

[0110] A "carrier" or "delivery vehicle" includes viral particles, viruses, polylysine compounds, and liposomes, which facilitate transfer of nucleic acid into cells. A carrier or delivery vehicle can also be used to deliver a protein or peptide to a cell.

[0111] Ranges: throughout this disclosure, various aspects of the embodiments can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range. Unless otherwise explicitly stated to the contrary, a range that is disclosed also includes the endpoints of the range.

[0112] Without being bound to any particular theory, the embodiments provided for herein have been found to show that a mutant VSV-G protein comprising a mutation at position 182 can be used to pseudotype a virus and transduce a cell when the virus comprises a targeting moiety. This mutation inhibits or reduces the VSV-G affinity to its natural co-receptor, the LDL-R. The mutant VSV-G proteins as provided can be used, in some embodiments, to transduce a target cell and deliver a heterologous molecule to the targeted cells.

[0113] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 198 as compared to SEQ ID NO: 1 or at position 182 as compared to SEQ ID NO: 2. SEQ ID NO: 1 is the full length protein and SEQ ID NO: 2 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MKCLLYLAFLFIGVNC (SEQ ID NO: 26) as shown at the N-terminus of SEQ ID NO: 1 is cleaved leaving a protein of SEQ ID NO: 2. Thus, although a mutation may be referred to in the context of SEQ ID NO: 2, it should be understood to also be made in the context of SEQ ID NO: 1, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 2. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a I182D mutation as compared to SEQ ID NO: 2. In some embodiments, the mutation is a I182E mutation as compared to SEQ ID NO: 2.

[0114] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 198 as compared to SEQ ID NO: 10 or at position 182 as compared to SEQ ID NO: 11. SEQ ID NO: 10 is the full length protein and SEQ ID NO: 11 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MLSYLIFALVVSPILG (SEQ ID NO: 27) as shown at the N-terminus of SEQ ID NO: 10 is cleaved leaving a protein of SEQ ID NO: 11. Thus, although a mutation may be referred to in the context of SEQ ID NO: 11, it should be understood to also be made in the context of SEQ ID NO: 10, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 11. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a T182D mutation as compared to SEQ ID NO: 11. In some embodiments, the mutation is a T182E mutation as compared to SEQ ID NO: 11.

[0115] In some embodiments, a VSV-G protein is provided that comprises a mutation at

position 198 as compared to SEQ ID NO: 12 or at position 182 as compared to SEQ ID NO: 13. SEQ ID NO: 12 is the full length protein and SEQ ID NO: 13 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MLRLFLFCFLALGAHS (SEQ ID NO: 28) as shown at the N-terminus of SEQ ID NO: 12 is cleaved leaving a protein of SEQ ID NO: 13. Thus, although a mutation may be referred to in the context of SEQ ID NO: 13, it should be understood to also be made in the context of SEQ ID NO: 12, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 13. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a A182D mutation as compared to SEQ ID NO: 13. In some embodiments, the mutation is a A182E mutation as compared to SEQ ID NO: 13.

[0116] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 203 as compared to SEQ ID NO: 14 or at position 182 as compared to SEQ ID NO: 15. SEQ ID NO: 14 is the full length protein and SEQ ID NO: 15 is the ectodomain of the VSV-G protein. The 21-mer signal peptide of MKMKMVIAGLILCIGILPAIG (SEQ ID NO: 29) as shown at the N-terminus of SEQ ID NO: 14 is cleaved leaving a protein of SEQ ID NO: 15. Thus, although a mutation may be referred to in the context of SEQ ID NO: 15, it should be understood to also be made in the context of SEQ ID NO: 14, which contains the leader sequence, and thus would be a position number that is 21 more than the position recited for SEQ ID NO: 15. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 15. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 15.

[0117] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 16 or at position 182 as compared to SEQ ID NO: 17. SEQ ID NO: 16 is the full length protein and SEQ ID NO: 17 is the ectodomain of the VSV-G protein. The 17-mer signal peptide of MTPAFILCMLLAGSSWA (SEQ ID NO: 30) as shown at the N-terminus of SEQ ID NO: 16 is cleaved leaving a protein of SEQ ID NO: 17. Thus, although a mutation may be referred to in the context of SEQ ID NO: 17, it should be understood to also be made in the context of SEQ ID NO: 16, which contains the leader sequence, and thus would be a

position number that is 17 more than the position recited for SEQ ID NO: 17. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 17. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 17.

[0118] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 18 or at position 182 as compared to SEQ ID NO: 19. SEQ ID NO: 18 is the full length protein and SEQ ID NO: 19 is the ectodomain of the VSV-G protein. The 17-mer signal peptide of MNFLLLTFIVLPLCSHA (SEQ ID NO: 31) as shown at the N-terminus of SEQ ID NO: 18 is cleaved leaving a protein of SEQ ID NO: 19. Thus, although a mutation may be referred to in the context of SEQ ID NO: 19, it should be understood to also be made in the context of SEQ ID NO: 18, which contains the leader sequence, and thus would be a position number that is 17 more than the position recited for SEQ ID NO: 19. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 19. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 19.

[0119] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 20 or at position 182 as compared to SEQ ID NO: 21. SEQ ID NO: 20 is the full length protein and SEQ ID NO: 21 is the ectodomain of the VSV-G protein. The 17-mer signal peptide of MLVLYLLLSLLALGAQC (SEQ ID NO: 32) as shown at the N-terminus of SEQ ID NO: 20 is cleaved leaving a protein of SEQ ID NO: 21. Thus, although a mutation may be referred to in the context of SEQ ID NO: 21, it should be understood to also be made in the context of SEQ ID NO: 20, which contains the leader sequence, and thus would be a position number that is 17 more than the position recited for SEQ ID NO: 21. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a I182D mutation as compared to SEQ ID NO: 21. In some embodiments, the mutation is a I182E mutation as compared to SEQ ID NO: 21.

[0120] As used herein, when a polypeptide is said to have a mutation as compared to a

reference sequence, such comparison is based on an alignment such as using BlastP or ClustalW or ClutalOmega alignment software using default parameters. For example, position 182 can be found in SEQ ID NO: 2 and also as compared to the other strains as illustrated in FIG. 3. FIG. 3 illustrates a clustal alignment of the wild-type sequences of the ectodomains of the various strains of the VSV-G protein. The residue that is bolded and underlined are the residues that align to position 182 of SEQ ID NO: 2 of the various strains. SEQ ID NO: 2 refers to ectodomain of the VSV-G protein of the Indiana strain. SEQ ID NO: 11 refers to ectodomain of the VSV-G protein of the New Jersey strain. SEQ ID NO: 13 refers to ectodomain of the VSV-G protein of the Marraba strain. SEQ ID NO: 15 refers to ectodomain of the VSV-G protein of the Carajas strain. SEQ ID NO: 17 refers to ectodomain of the VSV-G protein of the Alagoa strain. SEQ ID NO: 19 refers to ectodomain of the VSV-G protein of the Cocal strain. SEQ ID NO: 21 refers to ectodomain of the VSV-G protein of the Morreton strain. Accordingly, the residue that aligns to residues 182 as compared to SEQ ID NO: 2 can also be mutated as provided for herein.

[0121] In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is not an alanine. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is not a valine.

[0122] In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is I182S, I182H, I182T, I182Q, or I182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 11 is T182S, T182H, T182Q, or T182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 13 is A182S, A182H, A182T, A182Q, or A182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 15 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 17 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 19 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 21 is I182S, I182H, I182T, I182Q, or I182N. In some embodiments, the mutation at position 182 is not a hydrophobic residue. In some embodiments, the mutation at position 182 is a charged residue. In some embodiments, the mutation at position 182 is a negatively charged residue.

[0123] Although, the mutations may be described in reference to SEQ ID NO: 1 or SEQ

ID NO: 2, which is the VSV-G protein from the Indiana strain, the mutation can also be used in other strains of the VSV-G protein. For example, the mutation can be made in the New Jersey Strain of VSV-G, the Marraba strain of VSV-G, the Carajas strain of VSV-G, the Alagoa strain of VSV-G, the Cocal strain of VSV-G, or the Morreton strain of VSV-G. In some embodiments, the sequences of each are as provided herein. Examples of these can be found, for example in U.S. Patent Application Publication No. 20200216502, which is hereby incorporated by reference. For example, the wild-type full length or ectodomain of the New Jersey Strain of VSV-G are SEQ ID NO: 10 and SEQ ID NO: 11, respectively, the wild-type full length or ectodomain of Marraba strain of VSV-G are SEQ ID NO: 12 and SEQ ID NO: 13, respectively, the wild-type full length or ectodomain of Carajas strain of VSV-G are SEQ ID NO: 14 and SEQ ID NO: 15, respectively, the wild-type full length or ectodomain of Alagoa strain of VSV-G are SEQ ID NO: 16 and SEQ ID NO: 17, respectively, the wild-type full length or ectodomain of Cocal strain of VSV-G are SEQ ID NO: 18 and SEQ ID NO: 19, respectively, or the wild-type full length or ectodomain of Morreton strain of VSV-G are SEQ ID NO: 20 and SEQ ID NO: 21, respectively.

[0124] A VSV-G protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502, which is hereby incorporated by reference in its entirety. For example, the VSV-G protein can comprise a mutation at a position that corresponds to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2.

[0125] In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y. In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H. In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Q. In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y or H or Q. In some embodiments, the substitution at position 8 is selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glycine, isoleucine, valine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, or tryptophan. In some embodiments, the substitution at position 8 is selected from 8A, 8I, 8V, 8L,

and the like. In some embodiments, the substitution at position 8 is selected from H8A, H8I, H8V, H8L, and the like.

[0126] In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H. In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y. In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H or Y. In some embodiments, the substitution at position 209 is selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, isoleucine, valine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, or tryptophan.

[0127] In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K. In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except R. In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution at position 47 is selected from alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, valine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, or tyrosine. In some embodiments, the substitution at position 47 is selected from A, G, F, N, or Q. In some embodiments, the substitution at position 47 is selected from Q or N.

[0128] In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K. In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except R. In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution at position 354 is selected from alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, valine, leucine, methionine, phenylalanine,

proline, serine, threonine, tryptophan, or tyrosine. In some embodiments, the substitution at position 354 is selected from A, G, F, N, or Q.

[0129] In some embodiments, the substitution is at position 47 or at position 354, or at both positions 47 and 354 are, independently, substituted by A, G, F, N or Q. In some embodiments, the substitution at position 47 or at position 354, or at both positions 47 and 354 is, independently, A or Q or N.

[0130] In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to positions of 8, 47, 209 and/or 354. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein, at position 47 as provided for herein, at position 209 as provided for herein, and/or position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein and at position 47 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein and at position 209 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein and at position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 47 as provided for herein and at position 209 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 47 as provided for herein and at position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 209 as provided for herein and at position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein, at position 47 as provided for herein, and position 209 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein, at position 47 as provided for herein, and position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein, at position 209 as provided for herein, and position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 47 as provided for herein, at position 209 as provided for

herein, and position 354 as provided for herein. In some embodiments, the VSV-G protein can comprise a mutation at a position that corresponds to position 8 as provided for herein, at position 47 as provided for herein, at position 209 as provided for herein, and at position 354 as provided for herein.

[0131] In some embodiments, the substitution at position 8 is an alanine, i.e., H8A.

[0132] In some embodiments, the substitution at position 47 is Q or N or A, i.e., K47Q or K47N or K47A.

[0133] In some embodiments, the protein comprises a substitution at position 8 and/or a substitution at position 47. In some embodiments, the protein comprises a substitution at position 8 and a substitution at position 47. In some embodiments, the protein comprises a substitution at position 8 or a substitution at position 47. In some embodiments, the substitution at position 8 and/or a substitution at position 47 comprises a H8A and/or K47Q mutation.

[0134] In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[0135] In some non-limiting embodiments, the substitution at position 209 is A, i.e., Y209A.

[0136] In some non-limiting embodiments, the substitution at position 354 is A or Q, i.e. R354A or R354Q.

[0137] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 11 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 11 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0138] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 13 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 13 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0139] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 15 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 15 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0140] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 17 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 17 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0141] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 19 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 19 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0142] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 21 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 2020/0216502. For example, the VSV-G protein can comprise a mutation at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2. In some embodiments, the mutation in SEQ ID NO: 21 at a position analogous to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2 are as provided for herein.

[0143] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 2 (or SEQ ID NO: 1 if using the full length protein). In some embodiments, the protein is at least, or about, 80% identical to SEQ ID NO: 2. In some embodiments, the protein is at least,

or about, 85% identical to SEQ ID NO: 2. In some embodiments, the protein is at least, or about, 90% identical to SEQ ID NO: 2. In some embodiments, the protein is at least, or about, 95% identical to SEQ ID NO: 2. In some embodiments, the mutation at position 182 is I182D or I182E mutation. In some embodiments, the mutation is I182D. In some embodiments, the mutation is I182E mutation. In some embodiments, the mutation is I182S, I182H, I182T, I182Q, or I182N mutation.

[0144] In some embodiments, a VSV-G is provided wherein the protein comprises the amino acid sequence of SEQ ID NO: 2 with a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 2.

[0145] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 11 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 11 (or SEQ ID NO: 10 if using the full length protein). In some embodiments, the polypeptide comprises a T182D or T182E mutation. In some embodiments, the VSV-G protein comprises a T182S, T182H, T182Q, or T182N mutation.

[0146] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 13 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 13 (or SEQ ID NO: 12 if using the full length protein). In some embodiments, the polypeptide comprises a A182D or A182E mutation. In some embodiments, the VSV-G protein comprises a A182S, A182H, A182T, A182Q, or A182N mutation.

[0147] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 15 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 15 (or SEQ ID NO: 14 if using the full length protein). In some embodiments, the

polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0148] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 17 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 17 (or SEQ ID NO: 16 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0149] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 19 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 19 (or SEQ ID NO: 18 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0150] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 21 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 21 (or SEQ ID NO: 20 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or I182E mutation. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

Viral Particles

[0151] The mutant VSV-G proteins can be used, for example, to pseudotype a virus, such as, but not limited to a lentivirus. Accordingly, in some embodiments, a viral particle comprising a mutant VSV-G protein as provided herein are provided. In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 1. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%,

75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 2 (or SEQ ID NO: 1 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or I182E mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

[0152] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 10. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 11 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 11 (or SEQ ID NO: 10 if using the full length protein). In some embodiments, the polypeptide comprises a T182D or T182E mutation as compared to SEQ ID NO: 11. In some embodiments, the VSV-G protein comprises a T182S, T182H, T182Q, or T182N mutation.

[0153] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 12. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 13 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 13 (or SEQ ID NO: 12 if using the full length protein). In some embodiments, the polypeptide comprises a A182D or A182E mutation as compared to SEQ ID NO: 13. In some embodiments, the VSV-G protein comprises a A182S, A182H, A182T, A182Q, or A182N mutation.

[0154] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 203 as compared to SEQ ID NO: 14. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 15 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 15 (or SEQ ID NO: 14 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation

as compared to SEQ ID NO: 15. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0155] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 16. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 17 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 17 (or SEQ ID NO: 16 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation as compared to SEQ ID NO: 17. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0156] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 18. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 19 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 19 (or SEQ ID NO: 18 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation as compared to SEQ ID NO: 19. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[0157] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 20. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 21 comprises a mutation at position 182 and at least, or about, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical as compared to SEQ ID NO: 21 (or SEQ ID NO: 20 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or I182E mutation as compared to SEQ ID NO: 21. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

[0158] In some embodiments, the VSV-G protein further comprises a mutation at position

that corresponds to positions 214 and/or 352 of SEQ ID NO: 2. In some embodiments, the residue that corresponds to position 214 of SEQ ID NO: 2 is T214. In some embodiments, the residue that corresponds to position 352 of SEQ ID NO: is T352. In some embodiments, the VSV-G protein comprises mutation that corresponds to T214N mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises mutation that corresponds to T352A mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises a T214N and T352A mutations as compared to SEQ ID NO: 2. These mutations can be combined with any other mutations as provided for herein. In some embodiments, the T214N and/or T352A mutations are combined with the I182E or I182D mutations. In some embodiments, a VSV-G protein comprises an amino acid sequence of SEQ ID NO: 22 and SEQ ID NO: 23, which combines the I182D or I182E, respectively, with the T214N and T352A mutations. The sequences are also illustrated below with the leader sequences, which are removed during protein processing.

VSV-G Protein_ I196D, T230N and T368A mutations (with leader sequence and adjusted numbering)

MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIG
TALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQ
CKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVD
SQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLDSMDITFFSEDGELSSLGK
EGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPE
CPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKN
PGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYED
VEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDD
ESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHT
KKRQIYTDIEMNRLGK (SEQ ID NO: 24)

VSV-G Protein_I182D, T214N and T352A mutations (without leader sequence)

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQ
ADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNP
GFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTV

HNSTTWHSDYKVKGLCDSNLDSMDITFFSEDGELSSLGKEGTGFRSNYFAYENG
GKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVD
VSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKY
FETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDVEIGPNGVLRTSSGY
KFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPI
ELVEGWFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRL
GK (SEQ ID NO: 22)

VSV-G Protein with I196E, T230N and T368A mutations (with leader sequence and adjusted numbering)

MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIG
TALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQ
CKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVD
SQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLESMDITFFSEDGELSSLGK
EGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPE
CPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKN
PGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYED
VEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDD
ESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHT
KKRQIYTDIEMNRLGK (SEQ ID NO: 25)

VSV-G Protein with I182E, T214N and T352A mutations (without leader sequences)

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQ
ADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNP
GFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTV
HNSTTWHSDYKVKGLCDSNLESMDITFFSEDGELSSLGKEGTGFRSNYFAYENG
GKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVD
VSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKY
FETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDVEIGPNGVLRTSSGY
KFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPI

ELVEGWFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRL GK (SEQ ID NO: 23)

The other strains of the VSV-G protein as described herein can also comprises the mutations that correspond to T214N and/or T352A in SEQ ID NO: 2 and as illustrated in SEQ ID NO: 22 and SEQ ID NO: 23.

[0159] In some embodiments, the composition comprises a mutation as described in Hwang et al., Gene Ther 2013 Aug;20(8):807-15. (Epub 2013 Jan 31), which is hereby incorporated by reference in its entirety. For example, the mutations can be. at positions 230, 368, 66, and/or 162 that corresponds to SEQ ID NO: 1. The positions will be 16 positions less as compared to SEQ ID NO: 2, when the leader sequence is removed. In some embodiments, the mutations at those positions are, for example, T230N, T368A, K66T, S162T, or any combination thereof. In some embodiments, the VSV-G protein comprises a T230N and a T368A mutation. In some embodiments, the VSV-G polypeptide comprises a K66T, S162T, T230N, and a T368A. These positions are those that correspond to the positions in the full length protein (SEQ ID NO: 1). In some embodiments, the VSV-G protein comprises T230N mutation, a T368A mutation, a K66T mutation, a S162T mutation, or any combination thereof. In some embodiments, the VSV-G protein further comprises one or more mutations in addition to the mutation that corresponds to position 182 of SEQ ID NO: 2, such as those described in U.S. Patent Application Publication No. 20200216502, which is hereby incorporated by reference in its entirety. For example, the VSV-G protein can further comprise a mutation at a position that corresponds to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2.

[0160] In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y. In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H. In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution is at position 47

or at position 354, or at both positions 47 and 354 are substituted by A, G, F or Q. In some embodiments, the substitution is A or Q. In some embodiments, the substitution at position 8 is an alanine, i.e., H8A. In some embodiments, the substitution at position 47 is Q or N, i.e., K47Q or K47N. In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[0161] In some embodiments, the viral particle comprises a targeting moiety. The targeting moiety can be used to target the viral particle comprising the mutant VSV-G protein to a cell that expresses the target to which the targeting moiety binds to. In some embodiments, the targeting moiety is an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g., DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof. The targeting moiety can be attached to the viral surface through an IgG Fc stalk. In some embodiments, the stalk comprises a transmembrane domain. In some embodiments, the transmembrane domain comprises a CD8 transmembrane domain. In some embodiments, the transmembrane domain comprises a CD28 transmembrane domain. In some embodiments, the targeting moiety is attached (fused or linked) an envelope glycoprotein G or H of a virus of the Paramyxoviridae family, such as a morbillivirus, such as Measles virus, or a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus. In some embodiments, the targeting moiety can be attached (fused or linked) to a glycoprotein of a virus of the Rhabdoviridae family, such as a vesicular stomatitis New Jersey virus, a vesicular stomatitis Indiana virus, a vesicular stomatitis Alagoas virus, a vesicular stromatitis Maraba virus, a vesicular stomatitis Carajas virus, Parainfluenza virus, Spodoptera frugiperda rhabdovirus isolate Sf G, Drosophila obscura sigmavirus 10A, Wuhan insect virus 7, Perch virus, or Spring viremia of carp virus. In some embodiments, the VSV protein is the mutated proteins, such as those provided for herein. In some embodiments, the targeting moiety is attached to a glycoprotein of a virus of the Filoviridae family, such as Ebola virus or a glycoprotein of a virus of the Arenaviridae family, such as Machupo virus.

[0162] In some embodiments, the targeting moiety is a scFv. In some embodiments, the targeting moiety is a single domain antibody. In some embodiments, the targeting moiety is a VHH.

[0163] In some embodiments, the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34,

CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis

A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-l or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2

(RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1). In some embodiments, the targeting moiety binds to CD7. In some embodiments, the targeting moiety binds to CD8.

[0164] In some embodiments, the targeting moiety binds to a target that is present on a cell, such as an immune cell. In some embodiments, the cell is an immune cell, such as, but not limited to, T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte. In some embodiments, the cell is a T cell. In some embodiments, the cell is a B cell. In some embodiments, the cell is a CD7+ T cell and/or CD8+ T cell.

[0165] In some embodiments, the targeting moiety (a polypeptide) can bind to CD7.

[0166] In some embodiments, the polypeptide binds to CD7. In some embodiments, the polypeptide that binds to CD7 is an antibody which binds to non-human primate CD7. In some embodiments, the polypeptide that binds to CD7 is an antibody which binds to human CD7. The

sequence of human CD7 (UniProtKB P09564) is as follows (SEQ ID NO: 33):

MAGPPRLLLLPLLLALARGLPGALAAQEVQQSPHCTTVPVGASVNITCSTSGGLR
GIYLRQLGPQPQDIIYYEDGVVPTTDRRFRGRIDFSGSQDNLTITMHRLQLSDTGT
YTCQAITEVNVYGSGTLVLVTEEQSQGWHRCSDAPPRASALPAPPTGSALPDPQT
ASALPDPPAASALPAALAVISFLLGLGLGVACVLARTQIKKLCSWRDKNSAACV
VYEDMSHSRCNTLSSPNQYQ (SEQ ID NO: 33).

[0167] In some embodiments, the CD7 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is an immune cell. In some embodiments, the immune cell is a CD7+ T cell, CD4+ T cell, CD8+ T cell, NK cell, alpha-beta T cell, gamma-delta T cell, lymphoid progenitor cell, hematopoietic stem cell, myeloid cell, monocyte, macrophage, central memory T cell, effector memory T cell, stem-cell like memory T cells, naïve T cell, activated T cell, regulatory T cell (TReg), terminally differentiated effector memory T cell (TEMRA), resident memory T cell (TRM) or a T-cellCD8+CCR7+.

[0168] In some embodiments, the antibody comprises a Fc region. The Fc region can be linked to the heavy or light chain of the antibody. In some embodiments, the Fc region is an IgG Fc. In some embodiments, the IgG is selected from IgG1, IgG2, IgG3, or IgG4. In some embodiments, the IgG fc is IgG1 Fc. In some embodiments, the antibody comprises an Fc constant region of SEQ ID NO: 34 as set forth below.

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK (SEQ ID NO: 34)

[0169] In some embodiments, the IgG fc is IgG2 Fc. In some embodiments, the antibody comprises an Fc constant region of SEQ ID NO: 71 as set forth below.

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHN
AKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTK

GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 71)

[0170] In some embodiments, the IgG fc is IgG4 Fc. In some embodiments, the antibody comprises an Fc constant region of SEQ ID NO: 72 as set forth below.

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPA
PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVH
NAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKA
KGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
(SEQ ID NO: 72)

[0171] In some embodiments, polypeptides (e.g. CD7-binding polypeptide) are provided herein. In some embodiments, antibodies (*e.g.* an anti-CD7 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to CD7. In some embodiments, the CD7 protein is a human CD7 protein. In some embodiments, the CD7 protein is a non-human CD7 protein (e.g., mouse, rat, pig, dog, non-human primate). As used herein, the term "recombinant antibody" refers to an antibody that is not naturally occurring. In some embodiments, the term "recombinant antibody" refers to an antibody that is not isolated from a human subject.

[0172] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on Chothia numbering.

Chothia CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	HCDR3
CD7AB1	GYPFTSY (SEQ ID NO: 35)	DPNSGD (SEQ ID NO: 36)	SPYYSNDNSMDY (SEQ ID NO: 37)	RASQSIGTSIH (SEQ ID NO: 38)	YASESIS (SEQ ID NO: 39)	QQSNSWPTT (SEQ ID NO: 40)

[0173] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the

following table, which illustrate the CDRs based on Kabat numbering.

Kabat CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	HCDR3
CD7AB1	SYWIH (SEQ ID NO: 41)	RIDPNSGDT KYNEKFKN (SEQ ID NO: 42)	SPYYSNDNSM DY (SEQ ID NO: 37)	RASQSIGT SIH (SEQ ID NO: 38)	YASESIS (SEQ ID NO: 39)	QQSNSWPTT (SEQ ID NO: 40)

[0174] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on IMGT numbering.

IMGT CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
CD7AB1	GYPFTS YW (SEQ ID NO: 43)	IDPNSGDT (SEQ ID NO: 44)	ARSPYYSNDN SMDY (SEQ ID NO: 45)	QSIGTS (SEQ ID NO: 46)	YA	QQSNSWPTT (SEQ ID NO: 40)

[0175] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to non-human primate CD7. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to human CD7. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence selected from SEQ ID NO: 38-40. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 38. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 39. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 40. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence selected from SEQ ID NO: 35-37. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence

of SEQ ID NO: 35. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 36. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 37. The CDRs referenced in the embodiments throughout the present specification can be interchanged with the CDRs that are characterized by different formats, such as Kabat and IMGT.

[0176] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 38, the LCDR2 has a sequence of SEQ ID NO: 39, and the LCDR3 has a sequence of SEQ ID NO: 40.

[0177] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 46, the LCDR2 has a sequence of YA, and the LCDR3 has a sequence of SEQ ID NO: 40.

[0178] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 35, the HCDR2 has a sequence of SEQ ID NO: 36, and the HCDR3 has a sequence of SEQ ID NO: 37.

[0179] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 41, the HCDR2 has a sequence of SEQ ID NO: 42, and the HCDR3 has a sequence of SEQ ID NO: 37.

[0180] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 43, the HCDR2 has a sequence of SEQ ID NO: 44, and the HCDR3 has a sequence of SEQ ID NO: 45.

[0181] In some embodiments, a polypeptide, an antibody or antibody binding fragment thereof, comprises: (i) a light chain having any one of the foregoing recited combinations of LCDR1, LCDR2, and LCDR3 sequences; and (ii) a heavy chain having any one of the foregoing recited combinations of HCDR1, HCDR2, and HCDR3 sequences.

[0182] The different CDR motifs can be combined in any combination including those not depicted in the table above. For example, the following embodiments are provided as non-limiting examples of such combinations.

[0183] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37; or variants of any of the foregoing.

[0184] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 41; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 42; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37; or variants of any of the foregoing.

[0185] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 46; the light chain CDR2 has the amino acid sequence of YA; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 43; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 44; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 45; or variants of any of the foregoing.

[0186] In some embodiments, the light chain variable region CDR1 is replaced with any of the other light chain CDR1 sequences. In some embodiments, the light chain variable region CDR2 is replaced with any of the other light chain CDR2 sequences. In some embodiments, the light chain variable region CDR3 is replaced with any of the other light chain CDR3 sequences. In some embodiments, the heavy chain variable region CDR1 is replaced with any of the other heavy chain CDR1 sequences. In some embodiments, the heavy chain variable region CDR2 is replaced with any of the other heavy chain CDR2 sequences. In some embodiments, the heavy chain variable region CDR3 is replaced with any of the other heavy chain CDR3 sequences.

[0187] In some embodiments, the polypeptide comprises a heavy chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
47	CD7AB1	QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGL EWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSED SAVYYCARSPYYSNDNSMDYWGQGTSVTVSS

[0188] In some embodiments, the polypeptide comprises a light chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
48	CD7AB1	DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRTNDSPR LLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQ SNSWPTTFGGGTKLEIKR

[0189] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide of SEQ ID NO: 47. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_L peptide of SEQ ID NO: 48. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 47, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 47, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate CD7. In some embodiments, a polypeptide, an

antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 47, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human CD7. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence of SEQ ID NO: 48.

[0190] The VH and the VL sequences can be in any format, including, but not limited to an scFv format where the VH and VL regions are linked with a peptide linker. Examples of peptide linkers that can be used to link various peptides provided for herein include, but are not limited to: $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, the variable regions are not linked with a peptide linker. In some embodiments, the polypeptide comprises SEQ ID NO: 47 and SEQ ID NO: 48.

[0191] In some embodiments, the VH and VL polypeptides are linked to a Fc region. In some embodiments, the Fc region is as provided for herein. In some embodiments, the Fc region comprises an amino acid sequence of SEQ ID NO: 34, SEQ ID NO: 71, or SEQ ID NO: 72 as provided for herein. As provided for herein, the heavy chain can be linked to a Fc region. Non-limiting mutations in the Fc region are provided for herein. In some embodiments, the Fc region further comprises a transmembrane domain. Examples of transmembrane domains include, but are not limited to, a CD8 or CD28 ("CD8/CD28") transmembrane domain. In some embodiments, the Fc region further comprises a CD8 transmembrane domain. In some embodiments, the Fc region further comprises a CD28 transmembrane domain. In some embodiments, the Fc region comprising a transmembrane domain further comprises an Env incorporation motif. In some embodiments, the Fc region comprising a CD8/CD28 transmembrane domain further comprises an Env incorporation motif. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a transmembrane domain. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the VH and VL polypeptides provided herein linked to an Fc region

comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 47 and VL having a sequence as set forth in SEQ ID NO: 48 are linked to an Fc region comprising a transmembrane domain. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 47 and VL having a sequence as set forth in SEQ ID NO: 48 are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 47 and VL having a sequence as set forth in SEQ ID NO: 48 are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 47 and VL having a sequence as set forth in SEQ ID NO: 48 linked to an Fc region comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein.

[0192] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48 are linked to an Fc region comprising a transmembrane domain. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48 are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48 are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical

to a sequence of SEQ ID NO: 47; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48 linked to an Fc region comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein.

[0193] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48.

[0194] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 38-40; and/or a heavy chain CDR having a sequence of SEQ ID NO: 35-37. In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 38; a light chain CDR2 having a sequence of SEQ ID NO: 39; a light chain CDR3 having a sequence of SEQ ID NO: 40; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 35; a heavy chain CDR2 having a sequence of SEQ ID NO: 36; and a heavy chain CDR3 having a sequence of SEQ ID NO: 37. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0195] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 38; a LCDR2 having a sequence of SEQ ID NO: 39; and a LCDR3 having a sequence of SEQ ID NO: 40; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 35; a HCDR2 having a sequence of SEQ ID NO: 36; and a HCDR3 having a sequence of SEQ ID NO: 37.

[0196] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 38, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 39, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 40, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 35, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 36, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 37, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0197] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 38; a light chain CDR2 having a sequence of SEQ ID NO: 39; a light chain CDR1 having a sequence of SEQ ID NO: 40; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 41; a heavy chain CDR2 having a sequence of SEQ ID NO: 42; and a heavy chain CDR3

having a sequence of SEQ ID NO: 37. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0198] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 38; a LCDR2 having a sequence of SEQ ID NO: 39; and a LCDR3 having a sequence of SEQ ID NO: 40; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 41; a HCDR2 having a sequence of SEQ ID NO: 42; and a HCDR3 having a sequence of SEQ ID NO: 37.

[0199] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 38, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 39, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 40, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 41, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 42, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 37, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0200] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48;

provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 46; a light chain CDR2 having a sequence of YA; a light chain CDR1 having a sequence of SEQ ID NO: 40; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 43; a heavy chain CDR2 having a sequence of SEQ ID NO: 44; and a heavy chain CDR3 having a sequence of SEQ ID NO: 45. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0201] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 46; a LCDR2 having a sequence of YA; and a LCDR3 having a sequence of SEQ ID NO: 40; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 43; a HCDR2 having a sequence of SEQ ID NO: 44; and a HCDR3 having a sequence of SEQ ID NO: 45.

[0202] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 47; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 46, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of YA, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 40, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 43, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 44, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 45, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0203] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide,

wherein the V_H peptide comprises a sequence of SEQ ID NO: 47 and the V_L peptide comprises a sequence of SEQ ID NO: 48.

[0204] In some embodiments, a polypeptide as provided herein binds to non-human primate CD7. In some embodiments, a polypeptide as provided herein binds to human CD7.

[0205] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H-Z-V_L or V_L-Z-V_H, wherein Z is the peptide linker. In some embodiments, Z is $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

[0206] In some embodiments, a polypeptide comprising the linked peptide represented by a formula of V_L-Z-V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 47 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 50) to a light chain variable region as set forth in SEQ ID NO: 48. In some embodiments, a polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRTNDSPRLLIKYASESISGIP
SRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGTKLEIKRGGGGSGG
GGSGGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQR
PGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTS
EDSAVYYCARSPYYSNDNSMDYWGQGTSVTVSS (SEQ ID NO: 51).

[0207] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, a polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 51. In some embodiments, a polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 51. In some embodiments, a polypeptide comprises a sequence that is at least 99% identical to a sequence of

SEQ ID NO: 51. In some embodiments, a polypeptide comprises a sequence as set forth in SEQ ID NO: 51. In some embodiments, the polypeptide as set forth in SEQ ID NO: 51 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody.

[0208] In some embodiments, a polypeptide comprising the linked peptide represented by a formula of V_H-Z-V_L comprises a light chain variable region as set forth in SEQ ID NO: 48 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 50) to a heavy chain variable region as set forth in SEQ ID NO: 49. In some embodiments, a polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIDP
NSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSNDNS
MDYWGQGTSVTVSSGGGGSGGGGSGGGGSGGGGSDILLTQSPAILSVSPGERVS
FSCRASQSIGTSIHWYQQRTNDSPRLLIKYASESISGIPSRFSGSGSGTDFTLSINSV
ESEDIADYYCQQSNSWPTTFGGGTKLEIKR (SEQ ID NO: 52)

[0209] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52. In some embodiments, a polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 52. In some embodiments, a polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 52. In some embodiments, a polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 52. In some embodiments, a polypeptide comprises a sequence as set forth in SEQ ID NO: 52. In some embodiments, the polypeptide as set forth in SEQ ID NO: 52 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

[0210] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises an Fc region, such as those provided herein. In some

embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0211] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0212] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[0213] The sequences of the polypeptides or antibodies can be modified to yield human IgG antibodies. The conversion of the sequences provided herein can be modified to yield other types of antibodies. The CDRs can also be linked to other antibodies, proteins, or molecules to

create antibody fragments that bind CD7.

[0214] In some embodiments, a polypeptide or an antibody as provided herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD7 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the targeting moiety comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the targeting moiety comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 51. In some embodiments, the targeting moiety comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 51. In some embodiments, the targeting moiety comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the targeting moiety comprises a sequence as set forth in SEQ ID NO: 51. In some embodiments, the targeting moiety as set forth in SEQ ID NO: 51 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD7 antibody.

[0215] In some embodiments, a polypeptide or an antibody as provided for herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the engineered viral particle is a pseudotyped viral-like particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD7 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the targeting moiety comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 52. In some embodiments, the targeting moiety comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 52. In some embodiments, the targeting moiety comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 52. In some embodiments, the targeting moiety comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 52. In some embodiments, the targeting moiety comprises a sequence as set forth in SEQ ID NO: 52. In some embodiments, the targeting moiety as set forth in SEQ ID NO: 52 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some

embodiments, the anti-CD7 antibody binds to human CD7.

[0216] In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0217] In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 52 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 52 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0218] In some embodiments, the targeting moiety (a polypeptide) can bind to CD8.

[0219] In some embodiments, the polypeptide binds to CD8. In some embodiments, the polypeptide binds to CD8-alpha. In some embodiments, the polypeptide binds to CD8-beta. In some embodiments, the polypeptide binds to CD8 heterodimer. In some embodiments, the CD8 heterodimer comprises CD8-alpha and CD8-beta subunits. In some embodiments, the polypeptide binds to CD8-alpha homodimer. In some embodiments, the polypeptide that binds to CD8 is an antibody which binds to non-human primate CD8. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8-alpha. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to

non-human primate CD8-beta. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8-alpha homodimer. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8 heterodimer. In some embodiments, the polypeptide that binds to CD8 is an antibody which binds to human CD8. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-alpha. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-beta. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-alpha homodimer. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8 heterodimer. The sequence of human CD8-alpha (UniProtKB Q8TAW8) is as follows (SEQ ID NO: 53):

MALPVTALLLPLALLLHAARPSQFRVSPLDRTWNLGETVELKCQVLLSNPTSGCS
WLFQPRGAAASPTFLLYLSQNKPKAAEGLDTQRFSGKRLGDTFVLTLSDFRREN
EGCYFCSALSNSIMYFSHFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRP
AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNRRRVCKCPRP
VVKSGDKPSLSARYV (SEQ ID NO: 53).

[0220] The sequence of human CD8-beta (UniProtKB Q8TD28) is as follows (SEQ ID NO: 54):

MRPRLWLLLAAQLTVLHGNSVLQQTPAYIKVQTNKMVMLSCEAKISLSNMRIY
WLRQRQAPSSDSHHEFLALWDSAKGTIHGEEVEQEKIAVFRDASRFILNLTSVKP
EDSGIYFCMIVGSPELTFGKGTQLSVVDFLPTTAQPTKKSTLKKRVCRLPRPETQK
GPLCSPITLGLLVAGVLVLLVSLGVAIHLCCRRRRARLRFMKQLYK (SEQ ID NO: 54).

[0221] In some embodiments, the CD8 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is an immune cell. In some embodiments, the immune cell is a CD7+ T cell, CD4+ T cell, CD8+ T cell, NK cell, alpha-beta T cell, gamma-delta T cell, lymphoid progenitor cell, hematopoietic stem cell, myeloid cell, monocyte, macrophage, central memory T cell, effector memory T cell, stem-cell like memory T cells, naïve T cell,

activated T cell, regulatory T cell (TReg), terminally differentiated effector memory T cell (TEMRA), resident memory T cell (TRM) or a T-cellCD8+CCR7+. In some embodiments, the cell is a CD8+ T cell. In some embodiments, the cell is a CD8+ cell.

[0222] In some embodiments, the antibody comprises a Fc region. The Fc region can be linked to the heavy or light chain of the antibody. In some embodiments, the Fc region is an IgG Fc. In some embodiments, the IgG is selected from IgG1, IgG2, IgG3, or IgG4. In some embodiments, the IgG Fc is IgG1 Fc. In some embodiments, the antibody comprises an Fc constant region as set forth below.

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK (SEQ ID NO: 34)

[0223] In some embodiments, the IgG fc is IgG2 Fc. In some embodiments, the antibody comprises an Fc constant region of SEQ ID NO: 71 as set forth below.

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPA
PPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHN
AKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTK
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 71)

[0224] In some embodiments, the IgG fc is IgG4 Fc. In some embodiments, the antibody comprises an Fc constant region of SEQ ID NO: 72 as set forth below.

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
LQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPA
PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVH
NAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKA
KGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT

TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK (SEQ ID NO: 72)

[0225] In some embodiments, polypeptides (e.g. CD8-binding polypeptide) are provided herein. In some embodiments, antibodies (*e.g.* an anti-CD8 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to CD8. In some embodiments, the CD8 protein is a human CD8 protein. In some embodiments, the CD8 protein is a non-human CD8 protein (e.g., mouse, rat, pig, dog, non-human primate). As used herein, the term "recombinant antibody" refers to an antibody that is not naturally occurring. In some embodiments, the term "recombinant antibody" refers to an antibody that is not isolated from a human subject.

[0226] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on Chothia numbering.

Chothia CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	HCDR3
CD8AB1	RYTFTDY (SEQ ID NO: 55)	YPYNGG (SEQ ID NO: 56)	DHRYNEGVSFDY (SEQ ID NO: 57)	RASESVDGFGNSFMN (SEQ ID NO: 58)	LASNLES (SEQ ID NO: 59)	QQNNEDPYT (SEQ ID NO: 60)

[0227] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on Kabat numbering.

Kabat CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	HCDR3
CD8AB1	DYNLH (SEQ ID NO: 61)	FIYPYNGGTGYNQKFKN (SEQ ID NO: 62)	DHRYNEGVSFDY (SEQ ID NO: 57)	RASESVDGFGNSFMN (SEQ ID NO: 58)	LASNLES (SEQ ID NO: 59)	QQNNEDPYT (SEQ ID NO: 60)

[0228] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on IMGT numbering.

IMGT CDRs

Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
CD8AB1	RYTFTDYN(SEQ ID NO: 63)	IYPYNGGT (SEQ ID NO: 64)	ARDHRYNEGV SFDY (SEQ ID NO: 65)	ESVDGFGN SF (SEQ ID NO: 66)	LA	QQNNEDPYT (SEQ ID NO: 60)

[0229] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to non-human primate CD8. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to human CD8. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence selected from SEQ ID NO: 58-60. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 58. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 59. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 60. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence selected from SEQ ID NO: 55-57. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 55. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 56. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 57. The CDRs referenced in the embodiments throughout the present specification can be interchanged with the CDRs that are characterized by different formats, such as Kabat and IMGT.

[0230] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 58, the LCDR2 has a sequence of SEQ ID NO: 59, and the LCDR3 has a sequence of SEQ ID NO: 60.

[0231] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 66, the LCDR2 has a sequence of LA, and the LCDR3 has a sequence of SEQ ID NO: 60.

[0232] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 55, the HCDR2 has a sequence of SEQ ID NO: 56, and the HCDR3 has a sequence of SEQ ID NO: 57.

[0233] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 61, the HCDR2 has a sequence of SEQ ID NO: 62, and the HCDR3 has a sequence of SEQ ID NO: 57.

[0234] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 63, the HCDR2 has a sequence of SEQ ID NO: 64, and the HCDR3 has a sequence of SEQ ID NO: 65.

[0235] In some embodiments, a polypeptide, an antibody or antibody binding fragment thereof, comprises: (i) a light chain having any one of the foregoing recited combinations of LCDR1, LCDR2, and LCDR3 sequences; and (ii) a heavy chain having any one of the foregoing recited combinations of HCDR1, HCDR2, and HCDR3 sequences.

[0236] The different CDR motifs can be combined in any combination including those not depicted in the table above. For example, the following embodiments are provided as non-limiting examples of such combinations.

[0237] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 sequence

has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57; or variants of any of the foregoing.

[0238] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 61; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 62; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57; or variants of any of the foregoing.

[0239] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDRl, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 66; the light chain CDR2 has the amino acid sequence of LA; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 63; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 64; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 65; or variants of any of the foregoing.

[0240] In some embodiments, the light chain variable region CDR1 is replaced with any of the other light chain CDR1 sequences. In some embodiments, the light chain variable region CDR2 is replaced with any of the other light chain CDR2 sequences. In some embodiments, the light chain variable region CDR3 is replaced with any of the other light chain CDR3 sequences. In some embodiments, the heavy chain variable region CDR1 is replaced with any of the other heavy chain CDR1 sequences. In some embodiments, the heavy chain variable region CDR2 is replaced with any of the other heavy chain CDR2 sequences. In some embodiments, the heavy chain variable region CDR3 is replaced with any of the other heavy chain CDR3 sequences.

[0241] In some embodiments, the polypeptide comprises a heavy chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
67	CD8AB1	EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKLSHEKSL EWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSSTAYMELRSLTSVD AAVYYCARDHRYNEGVSFDYWGQGTTLTVSS

[0242] In some embodiments, the polypeptide comprises a light chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
68	CD8AB1	NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWYQQKPG QSPKLLIYLASNLESGVPARFSGSGSRTDFTLTIDPVEADDAATY YCQQNNEDPYTFGGGTKLEIKR

[0243] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide of SEQ ID NO: 67. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_L peptide of SEQ ID NO: 68. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 67, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 68, or a variant thereof. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 67, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 68, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate CD8. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 67, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 68, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human CD8. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence of SEQ ID NO: 68.

[0244] The VH and the VL sequences can be in any format, including, but not limited to an scFv format where the VH and VL regions are linked with a peptide linker. Examples of peptide linkers that can be used to link various peptides provided for herein include, but are not limited to: $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5. In some embodiments, n is 1.

In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, the variable regions are not linked with a peptide linker. In some embodiments, the polypeptide comprises SEQ ID NO: 67 and SEQ ID NO: 68.

[0245] In some embodiments, the VH and VL polypeptides are linked to a Fc region. In some embodiments, the Fc region is as provided for herein. As provided for herein, the heavy chain can be linked to a Fc region. Non-limiting mutations in the Fc region are provided for herein. In some embodiments, the Fc region further comprises a transmembrane domain. Examples of transmembrane domains include, but are not limited to, a CD8/CD28 transmembrane domain. In some embodiments, the Fc region further comprises a CD8 or CD28 ("CD8/CD28") transmembrane domain. In some embodiments, the Fc region further comprises a CD8 transmembrane domain. In some embodiments, the Fc region further comprises a CD28 transmembrane domain. In some embodiments, the Fc region comprising a transmembrane domain further comprises an Env incorporation motif. In some embodiments, the Fc region comprising a CD8/CD28 transmembrane domain further comprises an Env incorporation motif. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a transmembrane domain. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the VH and VL polypeptides provided herein are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the VH and VL polypeptides provided herein linked to an Fc region comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 67 and VL having a sequence as set forth in SEQ ID NO: 68 are linked to an Fc region comprising a transmembrane domain. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 67 and VL having a sequence as set forth in SEQ ID NO: 68 are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 67 and VL having a sequence as set forth in SEQ ID NO: 68 are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the VH having a sequence as set forth in SEQ ID NO: 67 and VL having a sequence

as set forth in SEQ ID NO: 68 linked to an Fc region comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein.

[0246] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68 are linked to an Fc region comprising a transmembrane domain. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68 are linked to an Fc region comprising a CD8/CD28 transmembrane domain. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68 are linked to an Fc region comprising a CD8/CD28 transmembrane domain and an Env incorporation motif. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68 linked to an Fc region comprising a CD8/CD28 transmembrane domain are anchored to the plasma membrane on the surface of a cell. In some embodiments, the cell is an immune cell, such as those provided herein.

[0247] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68.

[0248] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 58-60; and/or a heavy chain CDR having a sequence of SEQ ID NO: 55-57. In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 58; a light chain CDR2 having a sequence of SEQ ID NO: 59; a light chain CDR3 having a sequence of SEQ ID NO: 60; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 55; a heavy chain CDR2 having a sequence of SEQ ID NO: 56; and a heavy chain CDR3 having a sequence of SEQ ID NO: 57. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0249] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 58; a LCDR2 having a sequence of SEQ ID NO: 59; and a LCDR3 having a sequence of SEQ ID NO: 60; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 55; a HCDR2 having a sequence of SEQ ID NO: 56; and a HCDR3 having a sequence of SEQ ID NO: 57.

[0250] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67;

and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 58, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 59, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 60, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 55, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 56, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 57, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0251] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 58; a light chain CDR2 having a sequence of SEQ ID NO: 59; a light chain CDR3 having a sequence of SEQ ID NO: 60; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 61; a heavy chain CDR2 having a sequence of SEQ ID NO: 62; and a heavy chain CDR3 having a sequence of SEQ ID NO: 57. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0252] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 58; a LCDR2 having a sequence of SEQ ID NO: 59; and a LCDR3 having a sequence of SEQ ID NO: 60; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 61; a HCDR2 having a

sequence of SEQ ID NO: 62; and a HCDR3 having a sequence of SEQ ID NO: 57.

[0253] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 58, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 59, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 60, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 61, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 62, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 57, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0254] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 66; a light chain CDR2 having a sequence of LA; a light chain CDR3 having a sequence of SEQ ID NO: 60; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 63; a heavy chain CDR2 having a sequence of SEQ ID NO: 64; and a heavy chain CDR3 having a sequence of SEQ ID NO: 65. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[0255] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 66; a LCDR2 having a sequence of LA; and a LCDR3 having a sequence of SEQ ID NO: 60; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 63; a HCDR2 having a sequence of SEQ ID NO: 64; and a HCDR3 having a sequence of SEQ ID NO: 65.

[0256] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 67; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 68; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 66, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of LA, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 60, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 63, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 64, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 65, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[0257] In some embodiments, a polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence of SEQ ID NO: 67 and the V_L peptide comprises a sequence of SEQ ID NO: 68.

[0258] In some embodiments, a polypeptide as provided herein binds to non-human primate CD8. In some embodiments, a polypeptide as provided herein binds to human CD8.

[0259] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H-Z-V_L or

V_L-Z-V_H, wherein Z is the peptide linker. In some embodiments, Z is $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

[0260] In some embodiments, a polypeptide comprising the linked peptide represented by a formula of V_L-Z-V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 67 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 50) to a light chain variable region as set forth in SEQ ID NO: 68. In some embodiments, a polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWYQQKPGQSPKLLIYLA
SNLESGVPARFSGSGSRTDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEI
KRGGGGSGGGGSGGGGSGGGGSEVQLQQSGPELVKPGASVKISCKASRYTFTDY
NLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSSTAYMELRSL
TSVDAAVYYCARDHRYNEGVSFDYWGQGTTLTVSS (SEQ ID NO: 69).

[0261] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69. In some embodiments, a polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 69. In some embodiments, a polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 69. In some embodiments, a polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 69. In some embodiments, a polypeptide comprises a sequence as set forth in SEQ ID NO: 69. In some embodiments, the polypeptide as set forth in SEQ ID NO: 69 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD8 antibody.

[0262] In some embodiments, a polypeptide comprising the linked peptide represented by a formula of V_H-Z-V_L comprises a light chain variable region as set forth in SEQ ID NO: 68 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 50) to a heavy chain variable region as set forth in SEQ ID NO: 67. In some embodiments, a polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKLSHEKSLEWIGFIYPYN
GGTGYNQKFKNKAKLTVDYSSSTAYMELRSLTSVDAAVYYCARDHRYNEGVSF
DYWGQGTTLTVSSGGGGSGGGGSGGGGSGGGGSNIVLTQSPASLAVSLGQRATI
SCRASESVDGFGNSFMNWYQQKPGQSPKLLIYLASNLESGVPARFSGSGSRTDFT
LTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEIKR (SEQ ID NO: 70).

[0263] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70. In some embodiments, a polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 70. In some embodiments, a polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 70. In some embodiments, a polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 70. In some embodiments, a polypeptide comprises a sequence as set forth in SEQ ID NO: 70. In some embodiments, the polypeptide as set forth in SEQ ID NO: 70 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[0264] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env

incorporation motif.

[0265] In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0266] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[0267] The sequences of the polypeptides or antibodies can be modified to yield human IgG antibodies. The conversion of the sequences provided herein can be modified to yield other types of antibodies. The CDRs can also be linked to other antibodies, proteins, or molecules to create antibody fragments that bind CD8.

[0268] In some embodiments, a polypeptide or an antibody as provided herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD8 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the targeting moiety comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 69. In some embodiments, the targeting moiety comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 69. In some embodiments, the targeting moiety comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 69. In some embodiments, the targeting

moiety comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 69. In some embodiments, the targeting moiety comprises a sequence as set forth in SEQ ID NO: 69. In some embodiments, the targeting moiety as set forth in SEQ ID NO: 69 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD8 antibody.

[0269] In some embodiments, a polypeptide or an antibody as provided for herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the engineered viral particle is a pseudotyped viral-like particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD8 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the targeting moiety comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 70. In some embodiments, the targeting moiety comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 70. In some embodiments, the targeting moiety comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 70. In some embodiments, the targeting moiety comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 70. In some embodiments, the targeting moiety comprises a sequence as set forth in SEQ ID NO: 70. In some embodiments, the targeting moiety as set forth in SEQ ID NO: 70 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[0270] In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 69 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 69 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env

incorporation motif.

[0271] In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 70 and comprises an Fc region, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, and a transmembrane domain, such as those provided herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, and a CD8/CD28 transmembrane domain. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 70 and comprises an Fc region, such as those provided herein, a transmembrane domain, such as those provided herein, and an Env incorporation motif.

[0272] Although, the binders that bind to CD7 and CD8 are illustrated, in part, with a mutant VSV-G protein, other fusogenic proteins can also be used in place of the VSV-G protein. For example, in some embodiments, the pseudotyped viral-like particles can pseudotyped using viral glycoproteins other than VSV-G.

[0273] In some embodiments, viral particle can be pseudotyped using a viral glycoprotein from, for example, VSV. In some embodiments, viral particle can be pseudotyped using a viral glycoprotein from, for example, the Paramyxoviridae family. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of morbillivirus, such as Measles virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of the Measles virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of henipavirus, such as Nipah virus, Cedar virus, or Hendra virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of the Nipah virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to an envelope glycoprotein G or H of a virus of the Paramyxoviridae family. In some embodiments, the virus of the Paramyxoviridae family is a morbillivirus, such as Measles virus. In some embodiments, the virus of the Paramyxoviridae family is a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus.

[0274] In some embodiments, the pseudotyped viral-like particles comprising the targeting moieties provided for herein are pseudotyped with viral glycoproteins of viruses of the

Rhabdoviridae family. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of a vesicular stomatitis New Jersey virus, a vesicular stomatitis Indiana virus, a vesicular stomatitis Alagoas virus, a vesicular stromatitis Maraba virus, or a vesicular stomatitis Carajas virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to a glycoprotein of a virus of the Rhabdoviridae family. In some embodiments, the virus of the Rhabdoviridae family is the vesicular stomatitis New Jersey virus, the vesicular stomatitis Indiana virus, the vesicular stomatitis Alagoas virus, the vesicular stromatitis Maraba virus, or the vesicular stomatitis Carajas virus.

[0275] In some embodiments, the pseudotyped viral-like particles comprising the targeting moieties provided for herein are pseudotyped with viral glycoproteins of the Parainfluezna virus, Spodoptera frugiperda virus, Drosophila obscura sigmavirus, Wuhan insect virus 7, Spring viremia of carp virus, or Perch virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to a glycoprotein of a virus of the Rhabdoviridae family. In some embodiments, the virus of the Rhabdoviridae family is a Parainfluezna virus. In some embodiments, the virus of the Rhabdoviridae family is a Spodoptera frugiperda virus. In some embodiments, the virus of the Rhabdoviridae family is a Drosophila obscura sigmavirus. In some embodiments, the virus of the Rhabdoviridae family is a Wuhan insect virus 7. In some embodiments, the virus of the Rhabdoviridae family is a Spring viremia of carp virus. In some embodiments, the virus of the Rhabdoviridae family is a Perch virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to a Parainfluezna virus glycoprotein. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to a Spodoptera frugiperda rhabdovirus isolate Sf G virus glycoprotein.

[0276] In some embodiments, the pseudotyped viral-like particles comprising the targeting moieties provided for herein are pseudotyped with viral glycoproteins of viruses of the Arenaviridae family. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of the Machupo virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to a glycoprotein of a virus of the Arenaviridae family. In some embodiments, the virus of the Arenaviridae family is a Machupo virus.

[0277] In some embodiments, the viral particle comprising a mutant VSV-G protein (or other viral glycorptein) and/or or targeting moiety as provided for herein comprises a nucleic acid

molecule encoding for a heterologous molecule of interest or "cargo." For example, heterologous molecule of interest is meant to refer to any product that may be encoded by a nucleic acid molecule. As non-limiting examples, "cargo" or "heterologous molecule of interest" may refer to an siRNA, an shRNA, a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof. In some embodiments, the polypeptide is a chimeric antigen receptor ("CAR"). In some embodiments, the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, a chimeric antigen receptor ("CAR"), or a combination thereof. In some embodiments, the heterologous molecule of interest is a CAR.

[0278] A "chimeric antigen receptor" or "CAR" as used herein refers to an antigen-binding domain that is fused, directly, or indirectly (e.g. via a hinge or transmembrane domain to an intracellular signaling domain capable of activating or stimulating an immune cell. Most commonly, the CAR's extracellular binding domain is composed of a single chain variable fragment (scFv) derived from fusing the variable heavy and light regions of a murine or humanized monoclonal antibody. Alternatively, scFvs may be used that are derived from Fab's (instead of from an antibody, e.g., obtained from Fab libraries). In various embodiments, this scFv is fused to a transmembrane domain and then to an intracellular signaling domain. However, the antigen binding domain can be any molecule that can bind to the to target on the cell. For example, the antigen binding domain of a CAR can be an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g. DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof. In some embodiments, a CAR includes those that solely provide CD3ζ signals upon antigen binding. In some embodiments, the CAR includes those that provide both costimulation (e.g. CD28 or CD137) and activation (CD3 ζ). In some embodiments, the CARs include those that provide multiple costimulation (e.g. CD28 and CD137) and activation (CD3ζ). In various embodiments, the CAR is selected to have high affinity or avidity for the antigen. In some embodiments, the antigen-binding domain binds to CD20. In some embodiments, the antigen-binding domain comprises a CD20 antibody, or fragment thereof. In some embodiments, antibody fragments are as provided for herein, such as but not limited to a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g. DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof.

[0279] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, or a V_H and a V_L domain. In some embodiments, the V_H domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, or any value or range in-between.

EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISW NSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYY GMDVWGQGTTVTVSS (SEQ ID NO: 73)

In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 73. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 73. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 73. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 73. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 73.

[0280] In some embodiments, the V_L domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74, or any value or range in-between.

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRA TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTRLEIK (SEQ ID NO: 74)

In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 74. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 74. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 74. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 74. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 74.

[0281] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain and a V_L domain. In some embodiments, the V_H and V_L domain are not linked by a linker peptide. In some embodiments, the V_H and V_L domain are linked by a linker peptide, such as those as provided for herein, including but not limited to: $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5. In some embodiment n is 1. In some embodiment n is 2. In some embodiment n is 3. In some embodiment n is 4. In some embodiment n is 5.

[0282] In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having at least 90% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having at least 95% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having at least 98% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having at least 99% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 73, and comprises a V_L having the sequence of SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain

comprises a V_H domain having at least 90% identity to SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 73, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 73, and comprises a V_L having at least 90% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 73, and comprises a V_L having at least 90% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 73, and comprises a V_L having at least 95% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 73, and comprises a V_L having at least 95% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 73, and comprises a V_L having at least 98% identity to SEQ ID NO: 74. In some

embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 73, and comprises a V_L having at least 99% identity to SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 73, and comprises a V_L having an amino acid sequence of SEQ ID NO: 74.

[0283] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_L, wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 73, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 77), and V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 74. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_H-Z-V_L has an amino acid sequence as set forth below:

EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISW
NSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYY
GMDVWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCR
ASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEP
EDFAVYYCQQRSNWPITFGQGTRLEIK (SEQ ID NO: 75)

[0284] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 75. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 75. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 75. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 75. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 75. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 75.

[0285] In some embodiments, the antigen-binding domain of the CAR comprises a formula

of V_L-Z-V_H, wherein V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 74, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 77), and V_H is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 73. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L-Z-V_H has an amino acid sequence as set forth below:

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRA
TGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTRLEIKGGGGS
GGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPG
KGLEWVSTISWNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYC
AKDIQYGNYYYGMDVWGQGTTVTVSS (SEQ ID NO: 76)

[0286] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 76. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 76. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 76. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 76. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 76. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 76.

[0287] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, or a V_H and a V_L domain. In some embodiments, the V_H domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, or any value or range in-between.

DIVLTQSPAILSASPGEKVTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSNLAS
GVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSFNPPTFGGGTKLEIKGSTS
(SEQ ID NO: 78)

In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 78. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 78. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 78. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 78. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 78.

[0288] In some embodiments, the V_L domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79, or any value or range in-between.

EVQLQQSGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGQGLEWIGAIYP GNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSADYYCARSNYYGSSY WFFDVWGAGTTVTVSS (SEQ ID NO: 79)

In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 79. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 79. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 79. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 79. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 79.

[0289] In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L

having at least 90% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L having at least 95% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L having at least 98% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L having at least 99% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 78, and comprises a V_L having the sequence of SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the

CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 78, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 78, and comprises a V_L having at least 90% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 78, and comprises a V_L having at least 90% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 78, and comprises a V_L having at least 95% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 78, and comprises a V_L having at least 95% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 78, and comprises a V_L having at least 98% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 78, and comprises a V_L having at least 99% identity to SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 78, and comprises a V_L having an amino acid sequence of SEQ ID NO: 79.

[0290] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_L, wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 78, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 77), and V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 79. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_H-Z-V_L has an amino acid sequence as set forth below:

DIVLTQSPAILSASPGEKVTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSNLAS
GVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSFNPPTFGGGTKLEIKGSTS

GGGGSGGGGSGGGGSSEVQLQQSGAELVKPGASVKMSCKASGYTFTSYNMHW
VKQTPGQGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSED
SADYYCARSNYYGSSYWFFDVWGAGTTVTVSS (SEQ ID NO: 80)

[0291] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 80. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 80. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 80. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 80. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 80. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 80.

[0292] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_L-Z-V_H, wherein V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 79, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 77), and V_H is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 78. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L-Z-V_H has an amino acid sequence as set forth below:

SEVQLQQSGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGQGLEWIGAIY
PGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSADYYCARSNYYGSSY
WFFDVWGAGTTVTVSSGGGGSGGGGSGGGGSDIVLTQSPAILSASPGEKVTMTC
RASSSVNYMDWYQKKPGSSPKPWIYATSNLASGVPARFSGSGSGTSYSLTISRVE
AEDAATYYCQQWSFNPPTFGGGTKLEIKGSTS (SEQ ID NO: 81)

[0293] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 81. In some embodiments, the

antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 81. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 81. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 81. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 81. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 81.

[0294] In some embodiments, the antigen-binding domain of the CAR comprises rituximab, ocrelizumab, obinutuzumab, ofatumumab, ibritumomab tiuxetan, tositumomab, or ublituximab. In some embodiment, the antigen-binding domain comprises rituximab. In some embodiment, the antigen-binding domain comprises ofatumumab. In some embodiments, the CAR comprises the 4-1BB domain as well. These are merely illustrative in nature and are not limiting to the present embodiments and any chimeric antigen receptor can be delivered in conjunction with the viral particles and vectors provided for herein. These are non-limiting examples of CARs and any CAR construct could be encoded for by the nucleic acid molecule.

[0295] In some embodiments, the pseudotyped viral particle further comprises a heterologous nucleic acid molecule encoding a cargo of interest. The nucleic acid molecule may be useful for modulating the expression of a target gene. In some embodiments, the cargo can be used to modulate the activity of a cell or express a protein that is trafficked to the surface of the target cell. Therefore, in some embodiments, the nucleic acid may comprise an siRNA or an shRNA. The nucleic acid may also encode for a cargo of interest. Therefore, in some embodiments, the cargo of interest may comprise a polypeptide or portion thereof, a protein or portion thereof, a chimeric antigen receptor or portion thereof, or a tumor antigen or a portion thereof. In some embodiments, the cargo of interest is an antibody that is produced by the virus, which can then be secreted by the cell that is infected with the virus. The term "protein" can refer to any polypeptide that carries a native function in a cellular environment. Therefore, in some embodiments, the protein encoded by the nucleic acid cargo of interest may comprise an enzyme, a nuclear receptor, a transporter, a ribosomal protein, a membrane bound protein, a cytoplasmic protein, a G-protein coupled receptor, a voltage gated ion channel, a secretory protein, a

mitochondria protein, a cytokine, a chimeric antigen receptor, a tumor antigen, or a portion or chimeric species thereof.

[0296] Without being bound to any particular theory, the viral particle comprising the mutant VSV-G protein or other viral glycoprotein as provided for herein that comprises a targeting moiety can be used to express the heterologous molecule of interest in the target cell. Thus, for example, the CAR can be expressed in a T cell that is targeted by a viral particle pseudotyped with a VSV-G protein as provided for herein. Where the T cell is the intended target the viral particle can comprise a targeting moiety that binds to a target on the surface of a T cell, such as, but not limited to CD2, CD3, CD4, CD5, CD7 or CD8. In some embodiments, the target is CD2. In some embodiments, the target is CD3. In some embodiments, the target is CD4. In some embodiments, the target is CD5. In some embodiments, the target is CD6. In some embodiments, the target is CD7. In some embodiments, the target is CD8.

[0297] Also provided herein are viral particles comprising a targeting moiety that binds to CD7 or CD8, or a pharmaceutical composition comprising the same. In some the viral particle comprises a targeting moiety that binds to CD7. . In some the viral particle comprises a targeting moiety that binds to CD7.

[0298] In some embodiments, the viral particle that comprises a targeting moiety that binds to CD7 or CD8 is a pseudotyped viral particle. The viral particle can be pseudotyped with a viral glycoprotein, such as those, but not limited to, described herein. In some embodiments, the viral particle is pseudotyped with a VSV-G protein or mutant thereof, including, but not limited to, those provided for herein. The targeting moiety can be any antibody that or binder that binds to CD7 or CD8. Non-limiting examples are provided for herein.

[0299] In addition to being pseudotyped, the viral particles comprising a targeting moiety that binds to CD7 or CD8 can comprise a heterologous nucleic acid molecule encoding a molecule of interest. This can be, for example, a siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof. In some embodiments, the heterologous molecule of interest is a chimeric antigen receptor ("CAR").

[0300] In some embodiments, the pseudotyped viral particle is a recombinant lentivirus. In some embodiments, the recombinant pseudotyped viral particle is replication competent. In

some embodiments, the recombinant pseudotyped viral particle is replication incompetent.

[0301] In some embodiments, a pharmaceutical composition is provided comprising any composition, particle, or component provided for herein, such as an envelope pseudotyped viral particles or vectors as provided for herein, i.e. a particle that comprises a VSV-G mutant protein provided for herein or other viral glycoprotein, or particles that comprise a targeting moiety and/or a heterologous nucleic acid molecule as provided for herein.

[0302] In some embodiments, methods of delivering a cargo of interest to a cell are provided. In some embodiments, the methods comprise contacting the cell with the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same.

[0303] In some embodiments, methods of delivering a cargo of interest to a cell in a subject are provided. In some embodiments, the methods comprise administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same. In some embodiments, the cargo is a chimeric antigen receptor or as otherwise provided for herein.

[0304] In some embodiments, methods for of delivering a chimeric antigen receptor to a T-cell in a subject are provided. In some embodiments, the methods comprising administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same, wherein the pseudotyped viral-like particle or viral vector comprises a heterologous nucleic acid molecule encoding the chimeric antigen receptor.

[0305] Also provided herein are nucleic acid molecules encoding a mutant VSV-G protein as provided for herein.

[0306] Also provided herein are nucleic acid molecules encoding a targeting moiety, such as those provided for herein.

[0307] Methods of making the viral like particles or vectors are also provided. In some embodiments, the methods comprise making a viral like particles or vectors comprising a mutant VSV-G protein or other viral glycoprotein. In some embodiments, the methods comprise transfecting or transducing a packaging cell line with the nucleic acid molecules encoding a mutant VSV-G protein or another viral glycoprotein as provided for herein under conditions sufficient to

produce the pseudotyped viral-like particles or viral vectors. In some embodiments, the methods comprise transfecting or transducing a packaging cell line with the plurality of nucleic acid molecules provided for herein under conditions sufficient to produce the pseudotyped viral-like particles or viral vectors and optionally with a targeting moiety, such as one that binds to a target antigen, such as those provided for herein. In some embodiments, the targeting moiety binds to CD7 or CD8. In some embodiments, the targeting moiety comprises a sequence that binds to CD7 or CD8, such as those provided for herein. In some embodiments, methods further comprise isolating the pseudotyped viral-like particle or viral vector. In some embodiments, the nucleic acid molecules also comprise a nucleic acid molecule encoding a targeting moiety and/or a cargo that is to be delivered by the viral vector that is produced.

[0308] Accordingly, in some embodiments, cells are provided comprising heterologous nucleic acid molecules that encode the components to produce the virus. Packaging cell lines are known in the art and can be modified with the molecules of interest to produce the viral particle of interest.

[0309] For example, a cell or population of cells is provided that comprises one or more heterologous nucleic acid molecules encoding for a targeting moiety and/or a viral glycoprotein. In some embodiments, the cell comprises heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein. In some embodiments, the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety that binds to CD7 or CD8. In some embodiments, the targeting moiety that is encoded for comprises an amino acid sequence as provided for herein. In some embodiments, the viral glycoprotein encoded for is any viral glycoprotein that can function as a fusogenic protein to facilitate entry of the viral particle into a cell that expresses CD7 or CD8. In some embodiments, the viral glycoprotein is wild-type or a mutant VSV-G protein, such as those provided for herein. Other viral glycoproteins that can be encoded for are also described herein and can be used.

[0310] The viral particles provided for herein can be produced or made by, for example, culturing the cell under conditions sufficient to make the viral particle. In some embodiments, the cell is what is called a packaging cell line that provides components of the virus to produce the viral particle. These can be structural or non-structural viral components or proteins.

[0311] Also provided for herein are methods of treating cancer in a subject. In some

embodiments, the methods comprise administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same, wherein the pseudotyped viral-like particle or viral vector comprises a heterologous nucleic acid molecule encoding the chimeric antigen receptor.

[0312] Also provided herein are methods of treating a disease in a subject in need thereof.

[0313] In some embodiments, the methods provided include, but are not limited to, methods of treating a disease in a subject in need thereof, comprising administering to the subject the viral particle(s) provided herein to treat the disease.

[0314] In certain embodiments, the disease is a cancer. In addition, the compositions provided for herein can be used in methods for the treatment of any condition related to a cancer, such as a cell-mediated immune response against a tumor cell(s), where it is desirable to treat or alleviate the disease. The types of cancers to be treated include, but are not limited to, carcinoma, blastoma, sarcoma, certain leukemia or lymphoid malignancies, benign and malignant tumors, malignancies e.g., sarcomas, carcinomas, and melanomas. Other exemplary cancers include, but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer, thyroid cancer, and the like. In some embodiments, the cancer is the cancer is carcinoma, blastoma, sarcoma, leukemia, lymphoid malignancies, benign tumors, malignant tumors, sarcoma, carcinoma, melanoma, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer, thyroid cancer, B cell related cancer or T cell related cancer. The cancers may be non-solid tumors (such as hematological tumors) or solid tumors. Adult tumors/cancers and pediatric tumors/cancers are also included. In one embodiment, the cancer is a hematological tumor. In one embodiment, the cancer is a carcinoma. In one embodiment, the cancer is a sarcoma. In one embodiment, the cancer is a leukemia. In one embodiment the cancer is a solid tumor.

[0315] Solid tumors are abnormal masses of tissue that usually do not contain cysts or liquid areas. Solid tumors can be benign or malignant. Different types of solid tumors are named for the type of cells that form them (such as sarcomas, carcinomas, and lymphomas). Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma,

chondrosarcoma, osteosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, melanoma, CNS tumors (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma, germinoma, medulloblastoma, Schwannoma craniopharyogioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, neuroblastoma, retinoblastoma and brain metastases).

[0316] Carcinomas that can be amenable to therapy by the methods disclosed herein include, but are not limited to, esophageal carcinoma, hepatocellular carcinoma, basal cell carcinoma (a form of skin cancer), squamous cell carcinoma (various tissues), bladder carcinoma, including transitional cell carcinoma (a malignant neoplasm of the bladder), bronchogenic carcinoma, colon carcinoma, colorectal carcinoma, gastric carcinoma, lung carcinoma, including small cell carcinoma and non-small cell carcinoma of the lung, adrenocortical carcinoma, thyroid carcinoma, pancreatic carcinoma, breast carcinoma, ovarian carcinoma, prostate carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, renal cell carcinoma, ductal carcinoma in situ or bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical carcinoma, uterine carcinoma, testicular carcinoma, osteogenic carcinoma, epithelial carcinoma, and nasopharyngeal carcinoma.

[0317] In certain exemplary embodiments, the compositions provided herein can be used in methods to treat a myeloma, or a condition related to myeloma. Examples of myeloma or conditions related thereto include, without limitation, light chain myeloma, non-secretory myeloma, monoclonal gamopathy of undertermined significance (MGUS), plasmacytoma (e.g., solitary, multiple solitary, extramedullary plasmacytoma), amyloidosis, and multiple myeloma. In some embodiments, methods of treating multiple myeloma are provided. In some embodiments,

the multiple myeloma is refractory myeloma. In some embodiments, the multiple myeloma is relapsed myeloma.

[0318] In certain exemplary embodiments, the in vivo modified immune cells produced using the compositions provided herein are used to treat a melanoma, or a condition related to melanoma. Examples of melanoma or conditions related thereto include, without limitation, superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral lentiginous melanoma, amelanotic melanoma, or melanoma of the skin (e.g., cutaneous, eye, vulva, vagina, rectum melanoma). In some embodiments, the melanoma is cutaneous melanoma. In some embodiments, the melanoma is refractory melanoma. In some embodiments, the melanoma is relapsed melanoma.

[0319] In some embodiments, the compositions provided herein are used to treat a sarcoma, or a condition related to sarcoma. Examples of sarcoma or conditions related thereto include, without limitation, angiosarcoma, chondrosarcoma, chordoma, endotheliosarcoma, Ewing's sarcoma, fibrosarcoma, gastrointestinal stromal tumor, leiomyosarcoma, liposarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, mesothelioma, malignant peripheral nerve sheath tumor, myxosarcoma, osteogenic sarcoma, osteosarcoma, pleomorphic sarcoma, rhabdomyosarcoma, synovioma, synovial sarcoma, and other soft tissue sarcomas. In some embodiments, the sarcoma is synovial sarcoma. In some embodiments, the sarcoma is liposarcoma such as myxoid/round cell liposarcoma, differentiated/dedifferentiated liposarcoma, or pleomorphic liposarcoma. In some embodiments, the sarcoma is myxoid/round cell liposarcoma. In some embodiments, the sarcoma is refractory sarcoma. In some embodiments, the sarcoma is relapsed sarcoma.

[0320] In some embodiments, the subject has been treated with a therapeutic agent targeting the disease or condition, e.g. the tumor, prior to administration of the composition. In some aspects, the subject is refractory or non-responsive to the other therapeutic agent. In some embodiments, the subject has persistent or relapsed disease, e.g., following treatment with another therapeutic intervention, including chemotherapy, radiation, and/or hematopoietic stem cell transplantation (HSCT), e.g., allogenic HSCT. In some embodiments, the administration effectively treats the subject despite the subject having become resistant to another therapy.

[0321] In some embodiments, the subject is responsive to the other therapeutic agent, and

treatment with the therapeutic agent reduces disease burden. In some aspects, the subject is initially responsive to the therapeutic agent, but exhibits a relapse of the disease or condition over time. In some embodiments, the subject has not relapsed. In some such embodiments, the subject is determined to be at risk for relapse, such as at a high risk of relapse, and thus the composition is administered prophylactically, e.g., to reduce the likelihood of or prevent relapse. In some aspects, the subject has not received prior treatment with another therapeutic agent.

[0322] The administration of the compositions may be carried out in any convenient manner known to those of skill in the art. For example, the compositions may be administered to a subject by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a patient transarterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, intraperitoneally, intranasally, intracranially, or intraosseously. In other instances, the compositions are injected directly into a site of a local disease site in the subject, a lymph node, an organ, a tumor, and the like.

[0323] For the prevention or treatment of disease, the appropriate dosage may depend on the type of disease to be treated, the severity and course of the disease, whether the composition is administered for preventive or therapeutic purposes, previous therapy, the subject's clinical history and response to the treatment, and the discretion of the attending physician. The composition is, in some embodiments, suitably administered to the subject at one time or over a series of treatments.

[0324] In some embodiments, the composition is administered as part of a combination treatment, such as simultaneously with or sequentially with, in any order, another therapeutic intervention, such as an antibody or produced cell or receptor or agent, such as a cytotoxic or therapeutic agent. The composition(s), in some embodiments, is co-administered with one or more additional therapeutic agents or in connection with another therapeutic intervention, either simultaneously or sequentially in any order. In some contexts, the composition is co-administered with another therapy sufficiently close in time such that the composition enhances the effect of one or more additional therapeutic agents, or vice versa. In some embodiments, the composition is administered prior to the one or more additional therapeutic agents. In some embodiments, the composition is administered after the one or more additional therapeutic agents. In some

embodiments, the one or more additional agents includes a cytokine, such as IL-2, for example, to enhance persistence. In some embodiments, the methods comprise administration of a chemotherapeutic agent. In some embodiments, the methods do not comprise the administration of a chemotherapeutic agent.

[0325] In certain embodiments, the compositions may be administered to a subject in combination with an immune checkpoint antibody (e.g., an anti-PD1, anti-CTLA-4, or anti-PDL1 antibody). For example, viral vectors may be administered in combination with an antibody or antibody fragment targeting, for example, PD-1 (programmed death 1 protein). Examples of anti-PD-1 antibodies include, but are not limited to, pembrolizumab (KEYTRUDA®, formerly lambrolizumab, also known as MK-3475), and nivolumab (BMS-936558, MDX-1106, ONO-4538, OPDIVO®) or an antigen-binding fragment thereof. In certain embodiments, the compositions may be administered in combination with an anti-PD-L1 antibody or antigen-binding fragment thereof. Examples of anti-PD-L1 antibodies include, but are not limited to, BMS-936559, MPDL3280A (TECENTRIQ®, Atezolizumab), and MEDI4736 (Durvalumab, Imfinzi). In certain embodiments, the composition may be administered in combination with an anti-CTLA-4 antibody or antigen-binding fragment thereof. An example of an anti- CTLA-4 antibody includes, but is not limited to, Ipilimumab (trade name Yervoy). Other types of immune checkpoint modulators may also be used including, but not limited to, small molecules, siRNA, miRNA, and CRISPR systems. Immune checkpoint modulators may be administered before, after, or concurrently with the viral vector. In certain embodiments, combination treatment comprising an immune checkpoint modulator may increase the therapeutic efficacy of a therapy comprising a composition as provided herein. The other therapeutic can be administered simultaneously, before, or after the compositions provided herein are administered to the subject.

[0326] In certain embodiments, the subject is provided a secondary treatment. Secondary treatments include but are not limited to chemotherapy, radiation, surgery, and medications. In some embodiments, the subject is not provided a secondary treatment.

[0327] In some embodiments, the methods are performed without a lymphodepletion step, such as the administration of cyclophosphamide and/or fludarabine.

[0328] In some embodiments, the subject can be administered a conditioning therapy after the administration of the compositions to kill certain immune cells that are not transduced with the

CAR encoded by the compositions. This can be done by including a selection marker that is encoded by the nucleic acid cargo of interest. In some embodiments, the conditioning therapy comprises administering an effective amount of cyclophosphamide to the subject. In some embodiments, the conditioning therapy comprises administering an effective amount of fludarabine to the subject. In some embodiments, the conditioning therapy comprises administering an effective amount of a combination of cyclophosphamide and fludarabine to the subject.

[0329] In some embodiments, a specific dosage regimen of the present disclosure includes a lymphodepletion step after the administration of the composition. In an exemplary embodiment, the lymphodepletion step includes administration of cyclophosphamide and/or fludarabine.

[0330] In some embodiments, the lymphodepletion step includes administration of cyclophosphamide at a dose of between about 200 mg/m2/day and about 2000 mg/m2/day (e.g., 200 mg/m2/day, 300 mg/m2/day, or 500 mg/m2/day). In an exemplary embodiment, the dose of cyclophosphamide is about 300 mg/m2/day. In some embodiments, the lymphodepletion step includes administration of fludarabine at a dose of between about 20 mg/m2/day and about 900 mg/m2/day (e.g., 20 mg/m2/day, 25 mg/m2/day, 30 mg/m2/day, or 60 mg/m2/day). In an exemplary embodiment, the dose of fludarabine is about 30 mg/m2/day.

[0331] In some embodiment, the lymphodepletion step includes administration of cyclophosphamide at a dose of between about 200 mg/m2/day and about 2000 mg/m2/day (e.g., 200 mg/m2/day, 300 mg/m2/day, or 500 mg/m2/day), and fludarabine at a dose of between about 20 mg/m2/day and about 900 mg/m2/day (e.g., 20 mg/m2/day, 25 mg/m2/day, 30 mg/m2/day, or 60 mg/m2/day). In an exemplary embodiment, the lymphodepletion step includes administration of cyclophosphamide at a dose of about 300 mg/m2/day, and fludarabine at a dose of about 30 mg/m2/day.

[0332] In an exemplary embodiment, the dosing of cyclophosphamide is 300 mg/m2/day over three days, and the dosing of fludarabine is 30 mg/m2/day over three days.

[0333] It is known in the art that one of the adverse effects of the use of CAR T cells can be the onset of immune activation, known as cytokine release syndrome (CRS). CRS is immune activation resulting in elevated inflammatory cytokines. CRS is a known on-target toxicity, development of which likely correlates with efficacy. Clinical and laboratory measures range from

mild CRS (constitutional symptoms and/or grade-2 organ toxicity) to severe CRS (sCRS; grade ≥3 organ toxicity, aggressive clinical intervention, and/or potentially life threatening). Clinical features include: high fever, malaise, fatigue, myalgia, nausea, anorexia, tachycardia/hypotension, capillary leak, cardiac dysfunction, renal impairment, hepatic failure, and disseminated intravascular coagulation. Dramatic elevations of cytokines including interferon-gamma, granulocyte macrophage colony-stimulating factor, IL-10, and IL-6 have been shown following CAR T-cell infusion. One CRS signature is elevation of cytokines including IL-6 (severe elevation), IFN-gamma, TNF-alpha (moderate), and IL-2 (mild). Elevations in clinically available markers of inflammation including ferritin and C-reactive protein (CRP) have also been observed to correlate with the CRS syndrome. The presence of CRS generally correlates with expansion and progressive immune activation of adoptively transferred cells. It has been demonstrated that the degree of CRS severity is dictated by disease burden at the time of infusion as patients with high tumor burden experience a more sCRS.

[0334] Accordingly, in some embodiments, the methods comprise, following the diagnosis of CRS, appropriate CRS management strategies to mitigate the physiological symptoms of uncontrolled inflammation without dampening the antitumor efficacy of the in vivo generated cells (e.g., CAR T cells). CRS management strategies are known in the art. For example, systemic corticosteroids may be administered to rapidly reverse symptoms of sCRS (e.g., grade 3 CRS) without compromising initial antitumor response.

[0335] In some embodiments, an anti-IL-6R antibody may be administered. An example of an anti-IL-6R antibody is the Food and Drug Administration-approved monoclonal antibody tocilizumab, also known as atlizumab (marketed as Actemra, or RoActemra). Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R). Administration of tocilizumab has demonstrated near-immediate reversal of CRS.

[0336] CRS is generally managed based on the severity of the observed syndrome and interventions are tailored as such. CRS management decisions may be based upon clinical signs and symptoms and response to interventions, not solely on laboratory values alone.

[0337] Mild to moderate cases generally are treated with symptom management with fluid therapy, non-steroidal anti-inflammatory drug (NSAID) and antihistamines as needed for adequate symptom relief. More severe cases include patients with any degree of hemodynamic instability;

with any hemodynamic instability, the administration of tocilizumab is recommended. The first-line management of CRS may be tocilizumab, in some embodiments, at the labeled dose of 8 mg/kg IV over 60 minutes (not to exceed 800 mg/dose); tocilizumab can be repeated Q8 hours. If suboptimal response to the first dose of tocilizumab, additional doses of tocilizumab may be considered. Tocilizumab can be administered alone or in combination with corticosteroid therapy. Patients with continued or progressive CRS symptoms, inadequate clinical improvement in 12-18 hours or poor response to tocilizumab, may be treated with high-dose corticosteroid therapy, generally hydrocortisone 100 mg IV or methylprednisolone 1-2 mg/kg. In patients with more severe hemodynamic instability or more severe respiratory symptoms, patients may be administered high-dose corticosteroid therapy early in the course of the CRS. CRS management guidance may be based on published standards (Lee et al. (2019) Biol Blood Marrow Transplant, doi.org/10.1016/j.bbmt.2018.12.758; Neelapu et al. (2018) Nat Rev Clin Oncology, 15:47; Teachey et al. (2016) Cancer Discov, 6(6):664-679).

[0338] Features consistent with Macrophage Activation Syndrome (MAS) or Hemophagocytic lymphohistiocytosis (HLH) have been observed in patients treated with CAR-T therapy (Henter, 2007), coincident with clinical manifestations of the CRS. MAS appears to be a reaction to immune activation that occurs from the CRS, and should therefore be considered a manifestation of CRS. MAS is similar to HLH (also a reaction to immune stimulation). The clinical syndrome of MAS is characterized by high grade non-remitting fever, cytopenias affecting at least two of three lineages, and hepatosplenomegaly. It is associated with high serum ferritin, soluble interleukin-2 receptor, and triglycerides, and a decrease of circulating natural killer (NK) activity.

[0339] In some embodiments, methods of treating cancer in a subject in need thereof are provided, the methods comprising administering to the subject any of the compositions, such as the viral particle(s), provided herein.

[0340] The compositions disclosed herein can comprise a pharmaceutical composition, and for example include a pharmaceutically acceptable carrier, and/or a pharmaceutical formulation.

[0341] The term "pharmaceutical formulation" refers to a preparation which is in such form as to permit the biological activity of an active ingredient contained therein to be effective, and which contains no additional components which are unacceptably toxic to a subject to which

the formulation would be administered. A "pharmaceutically acceptable carrier" refers to an ingredient in a pharmaceutical formulation, other than an active ingredient, which is nontoxic to a subject. A pharmaceutically acceptable carrier includes, but is not limited to, a buffer, excipient, stabilizer, or preservative. In some aspects, the choice of carrier is determined in part by the particular cell and/or by the method of administration. Accordingly, there are a variety of suitable formulations. For example, the pharmaceutical composition can contain preservatives. Suitable preservatives may include, for example, methylparaben, propylparaben, sodium benzoate, and benzalkonium chloride. In some aspects, a mixture of two or more preservatives is used. The preservative or mixtures thereof are typically present in an amount of about 0.0001% to about 2% by weight of the total composition. Carriers are described, e.g., by Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980). Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and include, but are not limited to: buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g. Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG).

[0342] Buffering agents in some aspects are included in the compositions. Suitable buffering agents include, for example, citric acid, sodium citrate, phosphoric acid, potassium phosphate, and various other acids and salts. In some aspects, a mixture of two or more buffering agents is used. The buffering agent or mixtures thereof are typically present in an amount of about 0.001% to about 4% by weight of the total composition. Methods for preparing administrable pharmaceutical compositions are known. Exemplary methods are described in more detail in, for example, Remington: The Science and Practice of Pharmacy, Lippincott Williams & Wilkins; 21st

ed. (May 1, 2005).

[0343] The formulations can include aqueous solutions. The formulation or composition may also contain more than one active ingredient useful for the particular indication, disease, or condition being treated with the composition, preferably those with activities complementary to the composition, where the respective activities do not adversely affect one another. Such active ingredients are suitably present in combination in amounts that are effective for the purpose intended. Thus, in some embodiments, the pharmaceutical composition further includes other pharmaceutically active agents or drugs, such as chemotherapeutic agents, e.g., asparaginase, busulfan, carboplatin, cisplatin, daunorubicin, doxorubicin, fluorouracil, gemcitabine, hydroxyurea, methotrexate, paclitaxel, rituximab, vinblastine, and/or vincristine. The pharmaceutical composition in some embodiments contains the composition in amounts effective to treat or prevent the disease or condition, such as a therapeutically effective or prophylactically effective amount. Therapeutic or prophylactic efficacy in some embodiments is monitored by periodic assessment of treated subjects. The desired dosage can be delivered by a single bolus administration of the composition, by multiple bolus administrations of the composition, or by continuous infusion administration of the composition. In some embodiments, the pharmaceutical composition does not include a chemotherapeutic.

[0344] Formulations include those for oral, intravenous, intraperitoneal, subcutaneous, pulmonary, transdermal, intramuscular, intranasal, buccal, sublingual, or suppository administration. In some embodiments, the composition is administered parenterally. The term "parenteral," as used herein, includes intravenous, intramuscular, subcutaneous, rectal, vaginal, and intraperitoneal administration. In some embodiments, the composition is administered to the subject using peripheral systemic delivery by intravenous, intraperitoneal, or subcutaneous injection. Compositions in some embodiments are provided as sterile liquid preparations, e.g., isotonic aqueous solutions, suspensions, emulsions, dispersions, or viscous compositions, which may in some aspects be buffered to a selected pH. Liquid preparations are normally easier to prepare than gels, other viscous compositions, and solid compositions. Additionally, liquid compositions are somewhat more convenient to administer, especially by injection. Viscous compositions, on the other hand, can be formulated within the appropriate viscosity range to provide longer contact periods with specific tissues. Liquid or viscous compositions can comprise

carriers, which can be a solvent or dispersing medium containing, for example, water, saline, phosphate buffered saline, polyol (for example, glycerol, propylene glycol, liquid polyethylene glycol) and suitable mixtures thereof.

[0345] Sterile injectable solutions can be prepared by incorporating the composition in a solvent, such as in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose, dextrose, or the like. The compositions can contain auxiliary substances such as wetting, dispersing, or emulsifying agents (e.g., methylcellulose), pH buffering agents, gelling or viscosity enhancing additives, preservatives, flavoring agents, and/or colors, depending upon the route of administration and the preparation desired. Standard texts may in some aspects be consulted to prepare suitable preparations.

[0346] Various additives which enhance the stability and sterility of the compositions, including antimicrobial preservatives, antioxidants, chelating agents, and buffers, can be added. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, and sorbic acid. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

[0347] The formulations to be used for in vivo administration are generally sterile. Sterility may be readily accomplished, e.g., by filtration through sterile filtration membranes.

[0348] The embodiments provided for herein can be used for many purposes, since the a pseudotyped virus capable of fusing with a target cell can be used to deliver a gene or other heterologous sequence of interest.

ENUMERATED EMBODIMENTS

[0349] In some embodiments, the following embodiments are provided:

1. A VSV-G polypeptide comprising a mutation that corresponds to a mutation at position 182 of SEQ ID NO: 2.

2. The VSV-G polypeptide of embodiment 1, wherein the protein comprises an amino acid sequence of SEQ ID NO: 2 with a mutation at position 182 and has at least 70% identity to SEQ

ID NO: 2.

3. The VSV-G polypeptide of embodiments 1 or 2, wherein the polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.

4. The VSV-G polypeptide of any one of embodiments 1-3, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 1 with a mutation at position 198 and at least 70% identity to SEQ ID NO: 2.

5. The VSV-G polypeptide of any one of embodiments 1-4, wherein the polypeptide comprises a mutation that corresponds to I182D or I182E as compared to a sequence of SEQ ID NO: 2.

6. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises an amino acid sequence at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence of SEQ ID NO: 4.

7. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises a sequence of SEQ ID NO: 4.

8. The VSV-polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises an amino acid sequence at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence of SEQ ID NO: 5.

9. The VSV-G polypeptide of any one of embodiments 1-5, wherein the polypeptide comprises a sequence of SEQ ID NO: 5.

10. The VSV-G polypeptide of any one of embodiments 1-9, further comprising a mutation in

the VSV-G protein that corresponds to a mutation as described in US 2020/0216502, which is hereby incorporated by reference in its entirety.

11. The VSV-G polypeptide of any one of embodiments 1-10, further comprising a mutation in the VSV-G protein that corresponds to a position of 8, 10, 47, 209 and/or 354 as compared to SEQ ID NO: 2.

12. The VSV-G polypeptide of any one of embodiments 1-11, further comprising a mutation that corresponds to position 8 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except Y.

13. The VSV-G polypeptide of any one of embodiments 1-12, further comprising a mutation that corresponds to position 209 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except H.

14. The VSV-G polypeptide of any one of embodiments 1-13, further comprising a mutation that corresponds to position 47 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except K or R.

15. The VSV-G polypeptide of any one of embodiments 1-14, further comprising a mutation that corresponds to position 354 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except K or R.

16. The VSV-G polypeptide of any one of embodiments 1-15, further comprising a mutation that corresponds to position 10 in SEQ ID NO: 2, wherein the mutation is any amino acid different from the amino acid indicated at that position in SEQ ID NO: 2, except Q or N.

17. The VSV-G polypeptide of any one of embodiments 1-16, wherein the protein comprises a substitution at position 47 or at position 354, or at both positions 47 and 354, wherein each position is, independently, substituted by A, G, F, Q, or N.

18. The VSV-G polypeptide of any one of embodiments 1-17, wherein the protein comprises a substitution at position 8, wherein the substitution is H8A, H8I, H8V, H8L, and the like.

19. The VSV-G polypeptide of any one of embodiments 1-18, wherein the protein comprises a substitution at position 47, wherein the substitution is K47Q or K47N.

20. The VSV-G polypeptide of any one of embodiments 1-19, wherein the protein comprises a substitution H8A and/or K47Q mutation.

21. The VSV-G polypeptide of any one of embodiments 1-20, wherein the protein comprises a substitution at position 10, such as Q10A, Q10R, or Q10K substitution.

22. The VSV-G polypeptide of any one of embodiments 1-21, further comprising a mutation that corresponds to a mutation at positions 214 and/or 352 of SEQ ID NO: 2.

23. The VSV-G polypeptide of embodiment 22, wherein the polypeptide comprises a T214N and/or T352A mutation.

24. A VSV-G polypeptide comprising a substitution at positions I182 and at least one of T214, and T352 of SEQ ID NO: 2.

25. The VSV-G polypeptide of embodiment 24, wherein the polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2.

26. The VSV-G polypeptide of embodiments 24 or 25, wherein the substitution at position 182 is I182D or I182E, the substitution at position 214 is T214N, and the substitution at position 352 is T352A.

27. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide

comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25.

28. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 22.

29. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 23.

30. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 24.

31. The VSV-G polypeptide of any one of embodiments 24-26, wherein the polypeptide comprises a sequence of SEQ ID NO: 25.

32. A nucleic acid molecule encoding the VSV-G polypeptide of any one of embodiments 1-31.

33. A vector comprising the nucleic acid molecule of embodiment 32.

34. A plasmid comprising the nucleic acid molecule of embodiment 32.

35. A viral particle comprising the polypeptide of any one of embodiments 1-31.

36. The viral particle of embodiment 35, further comprising a targeting moiety.

37. The viral particle of embodiments 35 or 36, wherein the viral particle is a pseudotyped lentivirus.

38. The viral particle of any one of embodiments 35-37, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

39. The viral particle of embodiment 38, wherein the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof.

40. The viral particle of embodiments 38 or 39, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR").

41. The viral particle of any one of embodiments 35-40, wherein the targeting moiety binds to an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; "CD20+ cancer cell, CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

42. The viral particle of any one of embodiments 35-41, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123;

CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR);

Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-l or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein

72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1).

43. The viral particle of any one of embodiments 35-42, wherein the targeting moiety is an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g., DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof.

44. The viral particle of any one of embodiments 35-43, wherein the targeting moiety is attached to the viral surface through

an IgG Fc stalk;

an envelope glycoprotein G or H of a virus of the Paramyxoviridae family, such as a morbillivirus, such as Measles virus, or a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus;

a glycoprotein of a virus of the Rhabdoviridae family, such as a vesicular stomatitis New Jersey virus, a vesicular stomatitis Indiana virus, a vesicular stomatitis Alagoas virus, a vesicular stromatitis Maraba virus, a vesicular stomatitis Carajas virus, Parainfluenza virus, Spodoptera frugiperda rhabdovirus isolate Sf G, Drosophila obscura sigmavirus 10A, Wuhan insect virus 7, Perch virus, or Spring viremia of carp virus;

a glycoprotein of a virus of the Filoviridae family, such as Ebola virus; or

a glycoprotein of a virus of the Arenaviridae family, such as Machupo virus.

45. The viral particle of embodiment 44, wherein the stalk comprises a transmembrane domain, such as, but not limited to a CD8 or CD28 transmembrane domain.

46. A method of delivering a heterologous molecule to a target cell, the method comprising contacting the cell with a viral vector comprising:

a) the VSV-G protein of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

47. The method of embodiment 46, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

48. The method of embodiments 46 or 47, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1);

DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated

(MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-l or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1) on the target cell.

49. A method of delivering a heterologous molecule to a target cell in a subject, the method

comprising administering to the subject a viral vector comprising:

a) the VSV-G polypeptide of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

50. The method of embodiment 49, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

51. The method of embodiments 49 or 50, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC

epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen

recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-l or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family

Member 1A (XAGE1) on the target cell.

52. The method of any one of embodiments 46-51, wherein the heterologous molecule is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof, such as a chimeric antigen receptor ("CAR").

53. A method of treating cancer in a subject, the method comprising administering to the subject a viral vector comprising:

a) the VSV-G polypeptide of any one of embodiments 1-31;

b) a targeting moiety that binds to the target cell; and

c) a nucleic acid molecule encoding the heterologous molecule.

54. The method of embodiment 53, wherein the heterologous molecule is a chimeric antigen receptor.

55. The method of embodiments 53 or 54, wherein the target cell is an immune cell, such as a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.

56. The method of any one of embodiments 53-55, wherein the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3);

AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsgl); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-la); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of lmprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLll; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudinl8.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin Bl; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GMl; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(l-4)bDGlcp(l-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(l- 4)bDGlcp(l-l)Cer); GD3; GFRalpha4; Glycoprotein 100 (gplOO); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycoceramide (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLVl-Tax; Human papilloma virus E6

(HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; ILl lRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-llRa); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-l or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X

breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1) on the target cell.

57. The method of any one of embodiments 53-56, wherein the cancer is a cancer as provided for herein, such as a T cell or B cell disorder.

58. The viral particle of any one of embodiments 35-45, wherein the targeting moiety binds to CD7.

59. The viral particle of embodiment 58, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

60. The viral particle of embodiment 59, wherein the heavy chain comprises a heavy chain

variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

61. The viral particle of embodiments 59 and 60, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

62. The viral particle of any one of embodiments 59-61, wherein the polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

63. The viral particle of any one of embodiments 59-62, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

64. The viral particle of any one of embodiments 59-63, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

65. The viral particle of any one of embodiments 59-64, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99%

sequence identity to SEQ ID NO: 48.

66. The viral particle of any one of embodiments 59-65, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

67. The viral particle of any one of embodiments 59-66, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker, which can be for example, a glycine/serine linker.

68. The viral particle of embodiment 67, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein n is independently 1-5.

69. The viral particle of any one of embodiments 58-68, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

70. The viral particle of any one of embodiments 58-68, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

71. The viral particle of any one of embodiments 35-45, wherein the targeting moiety binds to CD8.

72. The viral particle of embodiment 71, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain

CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

73. The viral particle of embodiment 72, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

74. The viral particle of embodiment 72 or 73, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

75. The viral particle of any one of embodiments 72-74, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

76. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 90% sequence identity to

SEQ ID NO: 68.

77. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

78. The viral particle of any one of embodiments 72-75, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

79. The viral particle of embodiment 71, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

80. The viral particle of any one of embodiments 72-79, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker.

81. The viral particle of embodiment 80, wherein the peptide linker is a glycine/serine linker.

82. The viral particle of embodiments 80 or 81, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

83. The viral particle of any one of embodiments 71-82, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99%

sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

84. The viral particle of any one of embodiments 71-82, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

85. The method of any one of embodiments 46-57, wherein the targeting moiety that binds to the target cell binds to CD7.

86. The method of embodiment 85, wherein the targeting moiety comprises a polypeptide comprising: (i)a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

87. The method of embodiment 86, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

88. The method of embodiments 86 and 87, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

89. The method of any one of embodiments 86-88, wherein the polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

90. The method of any one of embodiments 86-89, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

91. The method of any one of embodiments 86-90, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

92. The method of any one of embodiments 86-91, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

93. The method of any one of embodiments 86-92, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

94. The method of any one of embodiments 86-93, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker, which

can be for example, a glycine/serine linker.

95. The method of embodiment 94, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein n is independently 1-5.

96. The method of any one of embodiments 85-95, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

97. The method of any one of embodiments 85-95, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

98. The method of any one of embodiments 46-57, wherein the targeting moiety that binds to the target cell binds to CD8.

99. The method of embodiment 98, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

100. The method of embodiment 99, wherein the targeting moiety comprises a heavy chain that

comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

101. The method of embodiment 99 or 100, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

102. The method of any one of embodiments 99-101, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

103. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

104. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

105. The method of any one of embodiments 99-102, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and

a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

106. The method of embodiment 98, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

107. The method of any one of embodiments 99-106, wherein the heavy chain variable region and the light chain variable region are, or are not, linked by a linker, such as a peptide linker.

108. The method of embodiment 107, wherein the peptide linker is a glycine/serine linker.

109. The method of embodiments 107 or 108, wherein the peptide linker comprises a sequence of $(GGGGS)_n$ (SEQ ID NO: 49), wherein each n is independently 1-5.

110. The method of any one of embodiments 98-109, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

111. The method of any one of embodiments 98-109, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

112. The viral particle of any one of embodiments 40-45 or 58-84, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 75.

113. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 75.

114. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 75.

115. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 75.

116. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 75.

117. The viral particle of embodiment 112, wherein the CAR comprises an antigen binding domain having an amino acid sequence having the amino acid sequence of SEQ ID NO: 75.

118. The viral particle of any one of embodiments 40-45 or 58-84, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 76.

119. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 76.

120. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 76.

121. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding

domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 76.

122. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 76.

123. The viral particle of embodiment 118, wherein the CAR comprises an antigen binding domain having an amino acid sequence having the amino acid sequence of SEQ ID NO: 76.

124. The method of any one of embodiments 46-57 or 85-111 wherein the heterologous molecule of interest is a chimeric antigen receptor (CAR), and wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 75.

125. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 75.

126. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 75.

127. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 75.

128. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 75.

129. The method of embodiment 124, wherein the CAR comprises an antigen binding domain having the amino acid sequence of SEQ ID NO: 75.

130. The method of any one of embodiments 46-57 or 85-111 wherein the heterologous molecule of interest is a chimeric antigen receptor (CAR), and wherein the CAR comprises an

antigen binding domain having an amino acid sequence having at least 85%. 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 76.

131. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 90% identity to SEQ ID NO: 76.

132. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 76.

133. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 98% identity to SEQ ID NO: 76.

134. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having an amino acid sequence having at least 99% identity to SEQ ID NO: 76.

135. The method of embodiment 130, wherein the CAR comprises an antigen binding domain having the amino acid sequence of SEQ ID NO: 76.

136. A viral particle comprising a targeting moiety that binds to CD7 or CD8, or a pharmaceutical composition comprising the same.

137. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light

chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing.

138. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

139. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

140. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

141. The viral particle of embodiment 137, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

141. The viral particle of embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

142. The viral particle embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

143. The viral particle embodiment 141, or a pharmaceutical composition comprising the same, wherein the light chain and a heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

144. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

145. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

146. The viral particle of embodiment 136, or a pharmaceutical composition comprising the same, wherein the targeting moiety binds to CD8.

147. The viral particle of embodiment 146, or a pharmaceutical composition comprising the

same, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

148. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

149. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

150. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

150. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

151. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

152. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

153. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

154. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

155. The viral particle of embodiment 146, or a pharmaceutical composition comprising the same, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

156. The viral particle of any one of embodiments 136-155, or a pharmaceutical composition comprising the same, wherein the viral particle is a lentivirus derived viral particle.

157. The viral particle of any one of embodiments 136-156, or a pharmaceutical composition comprising the same, wherein the viral particle comprises a heterologous fusogenic protein, such as a glycoprotein from such as those provided for herein .

158. The viral particle of embodiment 157, or a pharmaceutical composition comprising the same, wherein the fusogenic protein is a VSV-G protein.

159. The viral particle of embodiment 158, or a pharmaceutical composition comprising the same, wherein the VSV-G protein is a mutant VSV-G protein.

160. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the mutant VSV-G protein abrogates binding to its natural co-receptor, such as LDL-R.

161. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the mutant VSV-G protein comprises a polypeptide of any one of embodiments 1-30.

162. The viral particle of embodiment 159, or a pharmaceutical composition comprising the same, wherein the viral particle comprises a nucleic acid molecule encoding a chimeric antigen receptor.

163. The viral particle of embodiment 162, or a pharmaceutical composition comprising the same, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD20.

164. The viral particle of embodiment 163, or a pharmaceutical composition comprising the same, wherein the antigen binding domain that binds to CD20 comprises a VH and VL as provided for herein.

165. A method of delivering a heterologous molecule to a CD7+ or CD8+ target cell or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector comprising a targeting moiety that specifically binds to CD7 or CD8 on the target cell and a nucleic acid molecule encoding the heterologous molecule, wherein:

i) the targeting moiety that binds to CD7 comprises:

a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing;

a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37;

a light chain comprising: a light chain variable region having at least 90% sequence

identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40;

a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40;

a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48;

a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48;

a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48;

a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51; or

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52; or

ii) the targeting moiety that binds to CD8 comprises:

a polypeptide that comprises: a heavy chain variable region comprising heavy chain

CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing;

a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57;

a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60;

a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO:

67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68;

a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68;

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69; or

a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

166. The method of embodiment 165, wherein the pseudotyped viral particle is a pseudotyped lentivirus derived viral particle.

167. The method of embodiments 165 or 166,wherein the pseudotyped viral particle comprises a heterologous fusogenic protein, such as a glycoprotein from those provided for herein .

168. The method of embodiment 167,wherein the fusogenic protein is a VSV-G protein.

169. The method of embodiment 168, wherein the VSV-G protein is a mutant VSV-G protein.

170. The method of embodiment 169, wherein the mutant VSV-G protein abrogates binding to its natural co-receptor, such as LDL-R.

171. The method of embodiment 169, wherein the mutant VSV-G protein comprises a

polypeptide of any one of embodiments 1-30.

172. The method of any one of embodiments 165-171, wherein the heterologous nucleic acid molecule encodes for an siRNA, an shRNA, a non-coding RNA, a peptide, a polypeptide, a protein, a viral payload, a viral genome, a chimeric antigen receptor ("CAR") or a combination thereof.

173. The method of embodiment 172, wherein the heterologous nucleic acid molecule encodes for a chimeric antigen receptor.

174. The method of embodiment 173, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD20.

175. The method of embodiment 174, wherein the antigen binding domain that binds to CD20 comprises a VH and VL as provided for herein and linked polypeptides comprising the same.

176. A cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein.

177. The cell of embodiment 176, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety that binds to CD7 or CD8.

178. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising: (i)a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid

sequence of SEQ ID NO: 40; or variants of any of the foregoing.

179. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37.

180. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

181. The cell of embodiment 166, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40.

182. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting moiety that binds CD7 encodes for a polypeptide comprising a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48.

183. The cell of embodiment 177, wherein the nucleic acid molecule that encodes for a targeting

moiety that binds CD7 encodes for a polypeptide comprising a light chain and a heavy chain that comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48.

184. The cell of embodiment 183, wherein the light chain and the heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48.

185. The cell of embodiment 183, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48.

186. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

187. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD7 encodes for a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52.

188. The cell of embodiment 177, wherein the nucleic acid sequence encoding for a targeting moiety that binds to CD8.

189. The cell of embodiment 188, wherein the targeting moiety comprises a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDRl, CDR2, and CDR3

sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing.

190. The cell of embodiment 188, wherein the targeting moiety comprises a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57.

191. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

192. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60.

193. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable

region of the light chain having at least 90% sequence identity to SEQ ID NO: 68.

194. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68.

195. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68.

196. The cell of embodiment 188, wherein the CD8 targeting moiety comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68.

197. The cell of embodiment 188, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69.

198. The cell of embodiment 188, wherein the targeting moiety that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70.

199. The cells of any one of embodiments 176-198, wherein the heterologous nucleic acid molecule encoding the viral glycoprotein is a glycoprotein of any one of embodiments 1-30.

200. A cell comprising the nucleic acid molecule of embodiment 31, the vector of embodiment

32, or the plasmid of embodiment 33.

201. A method of making a viral particle comprising culturing the cell of any one of embodiments 176-198 under conditions sufficient to make the viral particle.

EXAMPLES

[0350] The following examples are illustrative, but not limiting, of the compounds, compositions, particles, polypeptids, and methods described herein. Other suitable modifications and adaptations known to those skilled in the art are within the scope of the following embodiments.

Example 1: Mutation at position 182 of VSV-G abrogates LDL-R interaction, but retains fusing properties.

[0351] **Plasmids/Sequences.** All VSV-G plasmids were derived from pCMV-VSV-G Envelope Vector (Cell Bio Labs, catalog RV-110). Point mutations and combinations thereof were introduced using site directed mutagenesis (New England Biolabs). Individual mutations H8A and K47Q were previously shown to partially "blind" VSV-G, reducing its binding to LDL-R, the native cellular receptor for VSV (PMID: 29531262, DOI: 10.1038/s41467-018-03432-4). In this experiment, a single binder molecule consisting of a CD7-targeting scFv (clone MT701) fused to an IgG "stalk" bearing a CD28 transmembrane domain was used.

[0352] **Cells**. HEK293T cells were grown in DMEM with 10% FBS. SupT1 cells were maintained in RPMI media with 10% FBS. Human PBMCs were purchased from AllCells and cultured in X-Vivo 10 (Lonza) supplemented with 20ng/mL IL-2 (Peprotech). PBMCs were activated 48 hours prior to transduction using anti-CD3/CD28 Dynabeads (Cell Therapy Systems).

[0353] **Generation of lentiviral particles**. The recombinant lentiviral particles co-expressing VSV-G glycoprotein and binder molecules were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total of 5 plasmids were transfected: (1) plasmid expressing the VSV-G glycoprotein, (2) plasmid expressing the binder protein (3) plasmid expressing the lentiviral transfer genome encoding for eGFP, (4) plasmid expressing gag-pol, and (5) plasmid expressing rev. Transfected cell supernatant was harvested 48 hours later. Virus in the cell supernatant was concentrated by centrifugation through a sucrose

cushion and resuspended in PBS. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[0354] **Lentivirus transduction assay**. A series of 10-fold dilutions (in cell culture media) of the concentrated lentivirus was performed and used to infect SupT1 and activated human PBMCs. Media was replaced 6 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with a viability stain and an anti-CD7 antibody to detect CD7 positive cells (PeCy7 mouse-anti-human CD7, clone CD7-6B7, BD Biosciences). Expression of eGFP was measured to calculate transduction efficiency.

[0355] **Structure-guided design of novel blinding mutations**. Using a published crystal structures of VSV-G bound to CR2 and CR3 of the LDL-R (pdb 50YL and 50Y9, respectively), we identified two putative positions in VSV-G with side chains oriented toward the binding interface on LDL-R (FIG. 1). Residue Q10 (SEQ ID NO: 2) appeared to form several interactions with residues in both CR2 and CR3. In CR3, this included interactions with a positively charged arginine residue. Thus, three substitutions were tested: Q10A to reduce side-chain interactions that potentially stabilize LDL-R binding and Q10R and Q10K to create electrostatic repulsion.

[0356] Residue I182 (SEQ ID NO: 2) appeared to contact several residues in both CR2 and CR3 as well. Three substitutions were tested: I182A to reduce side-chain interactions that potentially stabilize LDL-R binding and I182D and I182E to create electrostatic repulsion against the primary binding interfaces on LDL-R.

[0357] Addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. Titration of viral supernatants on the CD7+ T cell line SupT1 validated the structural predictions for residue I182. In the absence of any compensatory binder molecule, WT VSV-G reached titers of 3.0e8 while both I182D and I182E were ~3 orders of magnitude lower (Fig 2). Substitutions at residue I182 preserved fusogenicity, as titers were restored to 1e8 in the presence of a binder redirecting the virions to CD7.

[0358] The data is illustrated in FIG. 2, which shows that the addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. FIG.2A shows the titration of VSV-G constructs on SupT1 cells. Plotted is the percentage of SupT1 cells expressing GFP at each amount of viral input in terms of p24 antigen. Dashed lines/open circles indicate VSV-G constructs alone, solid lines/filled circles indicate the same construct with a CD7 targeting

molecule expressed in trans. FIG. 2B illustrates Functional titer of each construct calculated from the titration in A, expressed as transducing units per mL of concentrated virus supernatant (TU/mL).

[0359] Thus these examples demonstrate that a mutation at position 182 is sufficient to abrogate the LDL-R interaction, but retain fusogenic properties when combining with a targeting moiety that binds to a target on the target cell.

Example 2: Serum Stable VSV-G Protein

[0360] WT VSV-G is reported to be sensitive to inactivation by naïve human serum, with inactivation ranging from minimal change to about 100-fold decrease depending on study parameters. Accordingly, it was assessed i) whether substitution at position I182 produced a variant VSV-G with similar sensitivity to serum and ii) whether incorporation of known serum stabilizing VSV-G mutations into the I182 substituted constructs had an effect on the serum stability of the constructs.

[0361] WT VSV-G, Serum Stable VSV-G (T214N, T352A), LDL-R de-targeted VSV-G (I182E), and LDL-R de-targeted serum stable VSV-G (I182E, T214N, T352A) were tested for their ability to infect SupT1 cells in the presence or absence of naïve serum or heat inactivated serum (HI) (FIG. 4). As expected WT VSV-G had a dramatic decrease in percent infectivity when administered in the presence of serum with a mild rescue of infectivity if serum was heat inactivated (HI) (FIG. 4, columns 1-3). The inclusion of the CD7 targeting moiety on an IgG1 Fc stalk (WT) did not rescue the serum inactivation (FIG. 4, columns 4-6). The VSV-G constructs harboring the T214N and T352A mutations showed a similar reduction in infectivity in the presence of serum with no distinction between naïve or HI serum (FIG. 4, columns 7-9). However, the inclusion of the targeting moiety was able to partially rescue the inactivation in either serum condition (FIG. 4, columns 10-12). Surprisingly, the LDL-R de-targeted VSV-G (I182E) showed no reduction in infectivity percentage in the presence of either serum condition (FIG. 4, columns 13-15), but rather showed increased infectivity in the presence of naïve serum as compared to serum free or HI serum conditions. Further inclusion of the known serum stable mutations into VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in the presence of serum as compared to serum free conditions (FIG. 4, columns 16-18). Further, the I182E, T214N, T352A construct also demonstrates increased infectivity in the presence of HI serum (FIG. 4, column 18),

which indicates that the triple mutant construct has a higher degree of serum stability than the other constructs examined.

[0362] To further characterize the effect of including serum stabilizing mutations in the viral constructs of the present application, WT VSV-G, VSV-G (I182E), and VSV-G (I182E, T230N, T352A) were assessed at a lower dose of vector (FIG. 5). In agreement with the previous assessment, WT VSV-G showed decreased infectivity in serum as compared to no-serum conditions (FIG. 5, columns 1 and 2). However, heat inactivation (HI) of serum did appear to have a rescuing effect on WT VSV-G infectivity (FIG. 5, column 3). In further agreement with the previous assessment, VSV-G (I182E) demonstrated enhanced infectivity in the presence of serum as compared to no serum conditions (FIG. 5, columns 4 and 5). The presence of HI serum also resulted in an increased infectivity compared to no serum, with a smaller effect than naïve serum (FIG. 5, column 6). VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in serum and HI serum conditions as compared to no serum conditions (FIG. 5, columns 7-9), in agreement with the previous assessment. Further, when compared to the respective no serum condition, VSV-G (I182E, T230N, T352A) results in a greater percent increased infectivity compared to VSV-G (I182E), suggesting that inclusion of all three mutations results in greater serum stability than just I182E alone.

[0363] Thus, these examples demonstrate that i) the LDL-R detargeting mutation I182E affords an unexpected level of protection against the serum inactivation observed for WT VSV-G, ii) the LDL-R detargeting mutation I182E does not abrogate the serum stabilizing effect of the T230N + T352A mutations, and iii) the combined mutation construct VSV-G (I182E, T230N, T352A) appears to have a greater serum stabilizing effect than either I182E alone or T230N + T352A alone. Thus, VSV-G (I182E, T230N, T352A) is able to ablate native tropism without alternating fusogenicity and additionally demonstrates a more stable profile and is not neutralized in serum.

Example 3: CD7 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.

[0364] Generation of Plasmids and Sequences.

[0365] The amino acid sequence including CDRs of the CD7 binder was determined via mass spectrometry (Rapid Novor). CD7 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral

glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD7 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD7 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

[0366] Generation of Engineered Lentiviral Particles.

[0367] The recombinant lentiviral particles expressing the CD7 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the IgG stalk or a plasmid expressing the CD7 binder on a Nipah-G protein, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev.In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the Nipah-G protein, (2) plasmid expressing Nipah-F protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA)

[0368] CD7 binders attach to both human and non-human primate PBMCs, leading to CD7+ cell transduction.

[0369] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with an anti-CD7 antibody to detect CD7 positive cells (PE-Cy7 mouse-anti-human CD7, clone MT-701, Biolegend) as well as GFP expression. Cell viability was also determined. CD7 binders attached to Paramyxoviridae glycoproteins, such as Nipah-G (FIG. 6A-D and FIG. 7A-D) or with Rhabdoviridae glycoproteins, such as VSV-G (FIG. 6I-L and FIG. 7I-L) successfully transduced human PBMCs (FIG. 6A-L) or NHP PBMCs (FIG. 7A-L) compared to

the binder alone (FIG. 6E-H and FIG. 7E-H) which shows no transduction. When CD7 with an IgG stalk was tested, the binder alone (top row) again did not transduce human (FIG. 6M) or NHP PBMCs (FIG. 7M) but when administered with detargeted VSV-G, transduction was seen in both human (FIG. 6M, bottom panel) and NHP PBMCs (FIG. 7M, bottom panel). GFP transduction experiments were repeated as described above for detargeted VSV-G pseudotyped lentiviral constructs with CD7 binders. Results of the repeat experiments were in agreement with the data of FIGS 6 and 7 and are provided in Table 1 below.

TABLE 1

	WT VSVG	Detartgeted VSVG	CD7 Binder (SEQ ID NO. 51)	CD7 Binder (SEQ ID NO. 52)	CD8 Binder (SEQ ID NO. 69)	CD7 Binder (SEQ ID NO. 70)
Human PBMC Transduction (% positive)	52.76	0.00798	19.32	21.55	4.09	3.17
NHP PBMC Transduction (% positive)	48.4	0.026	2.61	5.64	1.8	0.76

[0370] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD7 and target viral particles to cells expressing CD7 to transduce the cells expressing CD7.

Example 4: CD8 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.

[0371] Generation of Plasmids and Sequences.

[0372] The amino acid sequence including CDRs of the CD8 binder was determined via mass spectrometry (Rapid Novor). CD8 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD8 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD8 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

[0373] Generation of Engineered Lentiviral Particles.

[0374] The recombinant lentiviral particles expressing the CD8 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD8 binder with the IgG stalk, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. In some embodiments, the lentiviral genome expressing eGFP was replaced with a CAR molecule. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[0375] CD8 binders attach to both human and non-human primate PBMCs, leading to CD8+ cell transduction.

[0376] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 6 after transduction. Cells were stained with an anti-CD8 antibody to detect CD8 positive cells (BV421 mouse-anti-human CD8, clone RPA-T8, Biolegend) as well as GFP or CAR20 expression. Cell viability was also determined. CD8 binders with detargeted VSV-G successfully transduced human PBMCs (FIG. 8A) or NHP PBMCs (FIG. 8B) with GFP (FIG. 8A-8B, top row) and CAR20 (FIG. 8A-8B, bottom row). GFP transduction experiments were repeated as described above for detargeted VSV-G pseudotyped lentiviral constructs with CD8 binders. Results of the repeat experiments were in agreement with the data of FIG 8 and are provided in Table 1 above.

[0377] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD8 and target viral particles to cells expressing CD8 to transduce the cells expressing CD8.

[0378] **Example 5: Binder construct affects transgene expression.**

[0379] Concentrated lentivirus was used to transduce SupT1 cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry. Cells were stained with an

anti-CD8 antibody to detect CD8 positive cells or an anti-CD7 antibody to detect CD7 positive cells as well as GFP or CAR20 expression.

[0380] Lentiviral constructs utilizing CD7 or CD8 binders as provided for herein exhibited comparable GFP transduction (FIG. 9A). Binder orientation (VH-VL vs VL-VH) had minimal effect on transgene expression. WT VSV-G was used as a positive control, and detargeted VSV-G was used as a negative control. With respect to a CD20-CAR transgene, lentiviral constructs utilizing CD7 binders as provided for herein provided superior transgene transduction as compared to lentiviral constructs utilizing CD8 binders (FIG. 9B). As with the GFP transgene, binder orientation had minimal effect on transgene expression. Lentiviral constructs utilizing CD7 or CD8 binders both demonstrated transgene expression levels near the level of WT VSV-G when greater amounts of virus were utilized.

[0381] These examples and embodiments demonstrate that the CD7 and CD8 binders of the present disclosure can be incorporated into a lentiviral particle to direct successful transgene expression in a target cell. Further, these examples and embodiments demonstrate that different binders result in differential transgene expression, and that both the identity of the binder and the identity of the transgene are important variable in the efficacy of the viral particle.

[0382] Example 6: VSV-G* pseudotyped lentiviruses harboring CD7 binder transduce PBMCs.

[0383] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. A CD7 binder construct was utilized in the present example. The CD7 binder was as provided for herein. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 10A) compared to the binder alone (FIG. 10B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 10C).

[0384] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses are able to successfully transduce a variety of human and non-human primate PMBCs.

[0385] Example 7: VSV-G* pseudotyped lentiviruses harboring a CD7 binder exhibit minimal off target transduction.

[0386] The off target transduction of B-cells via VSV-G* pseudotyped lentiviral constructs utilizing CD7 binders as provided for herein was assessed in several B-cell populations. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. B-cells cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect the various B-cell populations. A CD7 binder construct was utilized in the present example. The CD7 binder was as provided for herein. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 5 after transduction to determine GFP transduction. As a control, SupT1 cells were also infected with the same lentiviral constructs. None of the B-cell populations assessed demonstrated any significant level of GFP expression (FIG. 11A).

[0387] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner. VSV-G* pseudotyped lentiviruses utilizing the CD7 binder still exhibited minimal off target transduction of B-cells in all cell populations tested (FIG. 11B). The percent of CAR-T2A-GFP positive cells only exceeded 1% in line DB at the highest lentiviral concentrations utilized.

[0388] These examples and embodiments demonstrate that the i) VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure have low off target transduction of B-cells and ii) delivery of a CAR20 transgene instead of a GFP transgene does not significantly increase off target transduction in B-cells.

Example 8: VSV-G* pseudotyped lentiviruses with CD20-CAR transgene payload kills CD20 positive lymphoma cells *in vitro*

[0389] The ability of VSV-G* pseudotyped lentiviral constructs with a CD20-CAR transgene to kill CD20 positive lymphoma cells *in vitro* was assessed. The VSV-G* pseudotyped

lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Human PBMCs were transduced with a lentiviral construct carrying a CD20-CAR (CAR20) transgene. The CAR20 transgenes comprised antigen binding domains of SEQ ID NO: 75 or SEQ ID NO: 76. CD20 positive lymphoma cells were then added to the CAR20 cells at a given effector to target ratio (E:T). All lentiviral constructs tested produced a dose dependent killing of CAR20 positive lymphoma cells (FIG 12)

[0390] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure not only transduce the appropriate target cells as demonstrated by the previous examples, but also produce robust and dose dependent killing of CD20 positive lymphoma cells *in vivo*.

Example 9: VSV-G* pseudotyped lentiviruses deplete B-cells and eliminate established tumors in mice.

[0391] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was assessed. The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Mice were injected with lentiviral particles expressing a GFP transgene, or a CD20-CAR transgene. The mice utilized were huCD34 NSG mice which have circulating human T and B cells. Mice receiving lentiviral constructs expressing GFP saw no loss of CD20 (FIG. 13A) or CD19 (FIG. 13B) B cells. Mice receiving the CD20-CAR transgene saw a dramatic and sustained loss of B cells over three weeks as exhibited by a dramatic loss of both CD20 positive B cells (FIG. 13A) and CD19 positive B cells (FIG. 13B).

[0392] To further characterize the *in vivo* efficacy of the viral particles, the ability of VSV-G* pseudotyped lentiviral constructs to prevent tumor formation was assessed. Mice were injected with viral particles expressing a GFP transgene or a CD20-CAR transgene on protocol Day 1. On Day 9, mice were infused with Raji tumor cells and tumor progression was monitored. The experimental protocol illustrated in FIG. 14A. Mice receiving no treatment or lentiviral constructs

expressing GFP demonstrated progressive tumor development and spread as determined by IVIS imaging. In contrast, mice receiving lentiviral constructs expressing the CD20-CAR transgene demonstrated no tumor development after Raji cell infusion (FIG. 14B).

[0393] The ability of the viral particles to affect established tumors *in vivo* was also assessed. Mice were infused with Raji tumor cells on protocol Day 0. Mice were humanized via human PBMC engraftment on protocol Day 5, and mice were either not injected with viral particles (control) or injected with viral particles expressing a CD20-CAR transgene on protocol Day 6. Tumor progression was monitored through protocol Day 30. The experimental protocol is illustrated in FIG. 15A. Control and virus treated mice demonstrated comparable tumor load on Day 5 (prior to virus administration), Day 7, and Day 8 as determined by IVIS imaging, indicating that Raji tumors were established in both groups. At Day 12, control mice continued to exhibit increased tumor load, whereas virus treated mice exhibited a dramatic decrease in tumor load. The decreased tumor load was sustained throughout the duration of the experiment (FIG. 15B).

[0394] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviral constructs of the present disclosure are able to properly target B-cells *in vivo*, prevent tumor formation *in vivo*, and eliminate established tumors *in vivo*.

Example 10: VSV-G* pseudotyped lentiviruses deplete B-cells in non-human primates.

[0395] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was also assessed in non-human primates (Macaques). The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Macaques were injected with lentiviral particles on protocol Day 0 and their CD20+ cells were monitored. Injection of the lentiviral particles results in B-cell depletion in 6/6 Macaques tested.

[0396] This specification contains numerous citations to patents, patent applications, and publications. Each is hereby incorporated by reference for all purposes.

[0397] The specification also makes reference to various sequences, such as those provided

herein and below.

VSV-G Indiana Full length WT:
MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHA
SKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDE
YTGEWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETG
GKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIR
AGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIG
PNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWK
SSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 1)

VSV-G Indiana Ectodomain WT:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 2)

VSV-G Indiana ectodomain I182A:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNL[A]SMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 3)

VSV-G Indiana ectodomain I182D:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNL[D]SMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 4)

VSV-G Indiana ectodomain I182E:
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNL[E]SMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 5)

VSV-G Indiana ectodomain H8A + K47Q:
KFTIVFPANQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK

NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 6)

VSV-G Indiana ectodomain Q10A:
KFTIVFPHNAKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 7)

VSV-G Indiana ectodomain Q10R:
KFTIVFPHNRKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 8)

VSV-G Indiana ectodomain Q10K:
KFTIVFPHNKKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKY
ITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCS
NYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRL
PSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLY
MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLIIGL
FLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 9)

VSV-G New Jersey Full length WT:
MLSYLIFALVVSPILGKIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHS
ALWMTTCDFRWYGPKYITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAEAHIVTVTPHSVKVDE
YTGEWIDPHFIGGRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVST
EGICKMPFCRKPGYKLKNDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTW
SKIEAGEPITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYLRVELESPVIPRMEGKVAGTRIVRQLWDQWFPFGE
VEIGPNGVLKTKQGYKFPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGDTGVSKNPVELVE
GWFSGWRSSIMGVLAVIIGFVILIFLIRLIGVLSSLFRQKRRPIYKSDVEMAHFR (SEQ ID NO: 10)

VSV-G New Jersey ectodomain WT:
KIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHSALWMTTCDFRWYGPKY
ITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAEAHIVTVTPHSVKVDEYTGEWIDPHFIGGRCK
GQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVSTEGICKMPFCRKPGYKL
KNDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTWSKIEAGEPITPVDLSY
LGPKNPGAGPVFTIINGSLHYFMSKYLRVELESPVIPRMEGKVAGTRIVRQLWDQWFPFGEVEIGPNGVLKTKQGYK
FPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGDTGVSKNPVELVEGWFSGWRSSIMGVLAV
IIGFVILIFLIRLIGVLSSLFRQKRRPIYKSDVEMAHFR (SEQ ID NO: 11)

VSV-G Marraba Full length WT:
MLRLFLFCFLALGAHSKFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVSLHVKIPKSHKAIQADGWMCHA

AKWVTTCDFRWYGPKYITHSIHSMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAEVVVVQATPHHVLVDE
YTGEWIDSQLVGGKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTSLGKPNTGFRSNHFAYESG
EKACRMQYCTQWGIRLPSGVWFELVDKDLFQAAKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIR
AKLPVSPVDLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTMSGTTTERELWNDWYPYEDVEIG
PNGVLKTPTGFKFPLYMIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSSWK
STLASFFLIIGLGVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 12)

VSV-G Marraba ectodomain WT:
KFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVSLHVKIPKSHKAIQADGWMCHAAKWVTTCDFRWYGPKY
ITHSIHSMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAEVVVVQATPHHVLVDEYTGEWIDSQLVGGKCS
KEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTSLGKPNTGFRSNHFAYESGEKACRMQYCTQWGIRL
PSGVWFELVDKDLFQAAKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAKLPVSPVDLSYLAPK
NPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTMSGTTTERELWNDWYPYEDVEIGPNGVLKTPTGFKFPLY
MIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSSWKSTLASFFLIIGLGVAL
IFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 13)

VSV-G Carajas Full length WT:
MKMKMVIAGLILCIGILPAIGKITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLIDIGLRLRAPKSFKGISADG
WMCHAARWITTCDFRWYGPKYITHSIHSFRPSNDQCKEAIRLTNEGNWINPGFPPQSCGYASVTDSESVVVTVTKHQ
VLVDEYSGSWIDSQFPGGSCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPNSGIRSNYF
PYESLKDVCQMDFCKRKGFKLPSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSL
CQATWSKIQNKEALTPIDISYLGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGFVSGTSTSRVLWDQW
FPYGENSIGPNGLLKTASGYKYPLFMVGTGVLDADIHKLGEATVIEHPHAKEAQKVVDDSEVIFFGDTGVSKNPVEV
VEGWFSGWRSSLMSIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRRA (SEQ ID NO: 14)

VSV-G Carajas ectodomain WT:
KITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLIDIGLRLRAPKSFKGISADGWMCHAARWITTCDFRWYGPKY
ITHSIHSFRPSNDQCKEAIRLTNEGNWINPGFPPQSCGYASVTDSESVVVTVTKHQVLVDEYSGSWIDSQFPGGSCT
SPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPNSGIRSNYFPYESLKDVCQMDFCKRKGFKL
PSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSLCQATWSKIQNKEALTPIDISY
LGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGFVSGTSTSRVLWDQWFPYGENSIGPNGLLKTASGYK
YPLFMVGTGVLDADIHKLGEATVIEHPHAKEAQKVVDDSEVIFFGDTGVSKNPVEVVEGWFSGWRSSLMSIFGIILL
IVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRRA (SEQ ID NO: 15)

VSV-G Alagoa Full length WT:
MTPAFILCMLLAGSSWAKFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDLLGVNIRAKMPKVHKAIKADGWMCH
AAKWVTTCDYRWYGPQYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHSVMID
EYSGDWLDSQFPTGRCTGSTCETIHNSTLWYADYQVTGLCDSALVSTEVTFYSEDGLMTSIGRQNTGYRSNYFPYEK
GAAACRMKYCTHEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSLCQETWSKV
HSGLPISPVDLGYIAPKNPGAGPAFTIVNGTLKYFDTRYLRIDIEGPVLKKMTGKVSGTPTKRELWTEWFPYDDVEI
GPNGVLKTPEGYKFPLYMIGHGLLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKNPVEVIEGWFSNW
RSSVMAIVFAILLLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 16)

VSV-G Alagoa ectodomain WT:
KFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDLLGVNIRAKMPKVHKAIKADGWMCHAAKWVTTCDYRWYGPQY
ITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHSVMIDEYSGDWLDSQFPTGRCT
GSTCETIHNSTLWYADYQVTGLCDSALVSTEVTFYSEDGLMTSIGRQNTGYRSNYFPYEKGAAACRMKYCTHEGIRL
PSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSLCQETWSKVHSGLPISPVDLGYIAPK
NPGAGPAFTIVNGTLKYFDTRYLRIDIEGPVLKKMTGKVSGTPTKRELWTEWFPYDDVEIGPNGVLKTPEGYKFPLY
MIGHGLLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKNPVEVIEGWFSNWRSSVMAIVFAILLLVIT

VLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 17)

VSV-G Cocal Full length WT:
MNFLLLTFIVLPLCSHAKFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQADGWMCH
AAKWITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDSVAVVVQATPHHVLVD
EYTGEWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPNTGYRSNYFAYEK
GDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKI
RSKQPVSPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEI
GPNGILKTPTGYKFPLFMIGHGMLDSDLHKTSQAEVFEHPHLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSW
KSTVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 18)

VSV-G Cocal ectodomain WT:
KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQADGWMCHAAKWITTCDFRWYGPKY
ITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDSVAVVVQATPHHVLVDEYTGEWIDSQFPNGKCE
TEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPNTGYRSNYFAYEKGDKVCKMNYCKHAGVRL
PSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPK
NPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEIGPNGILKTPTGYKFPLF
MIGHGMLDSDLHKTSQAEVFEHPHLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSWKSTVVTFFFAIGVFILL
YVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 19)

VSV-G Morreton Full length WT:
MLVLYLLLSLLALGAQCKFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWHNGLIGTSLQVKMPKSHKAIQADGWMCH
AAKWVTTCDFRWYGPKYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAEAVIVKATPHQVLVD
EYTGEWVDSQFPTGKCNKDICPTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYEN
GDKACRMQYCKHWGVRLPSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKI
RAHLPISPVDLSYLSPKNPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEI
GPNGVLKTATGYKFPLYMIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGW
KSTIASFFFIIGLVIGLYLVLRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 20)

VSV-G Morreton ectodomain WT:
KFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWHNGLIGTSLQVKMPKSHKAIQADGWMCHAAKWVTTCDFRWYGPKY
VTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAEAVIVKATPHQVLVDEYTGEWVDSQFPTGKCN
KDICPTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYENGDKACRMQYCKHWGVRL
PSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAHLPISPVDLSYLSPK
NPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEIGPNGVLKTATGYKFPLY
MIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGWKSTIASFFFIIGLVIGL
YLVLRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 21)

Fc IgG1 (Accession No. P01857)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)

Fc IgG2 (Accession No. AAN76043)
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFN
WYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPP
SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE

ALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

Fc IgG4 (Accession No. AAB59394)
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
KTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF
NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLP
PSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH
EALHNHYTQKSLSLSLGK (SEQ ID NO: 28)

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that

This declaration is directed to:

- ☐ The attached application, or
- ■ United States application or PCT international application number 18/066,420 filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Ronnie M. Russell Date (Optional): January 5, 2023

Signature: Ronnie M. Russell

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Philip R. Johnson Date (Optional): Jan 17, 2023

Signature: [signature]

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420

filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: James I. Andorko Date (Optional): 1/5/23

Signature: James I. Andorko

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (08-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Mohit Sachdeva Date (Optional): June 20 2023

Signature: M Sachdeva

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Bruce Schnepp Date (Optional): Jan 5, 2023

Signature: Bruce E Schnepp

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420

filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Michael Marinelli Date (Optional): 1/10/23

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2036. OMB 0651-0032
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Jeffrey Foss Date (Optional): 1/10/23

Signature: [signature]

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Debasish Boral Date (Optional): Jan 5 2023

Signature: Debasish Boral

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**04/24/2023 03:17:14 PM ET**	**148165.001401**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Madison Sauer
PATENT CENTER #	61972679	FILING DATE	12/15/2022
CUSTOMER #	78442	FIRST NAMED INVENTOR	Ronnie M. Russell
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Daniel Scolnick

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
INH-014US Declarations filed April 24 2023.pdf	8	Oath or Declaration filed	3549 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
INH-014US Declarations filed April 24 2023.pdf	03F5EA24011EBC7AE430DC170C275CB5FBDD7FA93054093C 6FE496AFE08E87DA6DA583ADDB64FE48480623FB5060A980D CE7C8BE4B653396DC1F174CD7C605F6

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that

This declaration is directed to:

- ☐ The attached application, or
- ■ United States application or PCT international application number 18/066,420 filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Ronnie M. Russell Date (Optional): January 5, 2023

Signature: Ronnie M. Russell

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420

filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Philip R. Johnson Date (Optional): Jan 17, 2023

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420

filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: James I. Andorko Date (Optional): 1/5/23

Signature: James I. Andorko

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (08-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Mohit Sachdeva Date (Optional): June 20 2023

Signature: M Sachdeva

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Bruce Schnepp Date (Optional): Jan 5, 2023

Signature: Bruce E Schnepp

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that

This declaration is directed to:

- ☐ The attached application, or
- ☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Michael Marinelli Date (Optional): 1/10/23

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2036. OMB 0651-0032
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Jeffrey Foss Date (Optional): 1/10/23

Signature: [signature]

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/01 (06-12)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 18/066,420 filed on December 15, 2022.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Debasish Boral Date (Optional): Jan 5 2023

Signature: [signature]

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**05/10/2023 04:15:21 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Madison Sauer
PATENT CENTER #	62070053	FILING DATE	12/15/2022
CUSTOMER #	51414	FIRST NAMED INVENTOR	Ronnie M. Russell
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Christopher Bodle

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
INH-014USC1 Declarations as filed.pdf	8	Oath or Declaration filed	3549 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
INH-014USC1 Declarations as filed.pdf	03F5EA24011EBC7AE430DC170C275CB5FBDD7FA93054093C6FE496AFE08E87DA6DA583ADDB64FE48480623FB5060A980DCE7C8BE4B653396DC1F174CD7C605F6

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/066,420	12/15/2022	Ronnie M. Russell	148165.001401

CONFIRMATION NO. 1909

78442
Troutman Pepper Hamilton Sanders LLP
899 Cassatt Road
400 Berwyn Park
Berwyn, PA 19312

POWER OF ATTORNEY NOTICE

OC000000056982522

Date Mailed: 05/12/2023

NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/06/2023.

- The Power of Attorney to you in this application has been revoked by the applicant. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/ttran/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US

CONFIRMATION NO. 1909

51414
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

POA ACCEPTANCE LETTER

OC000000056982634

Date Mailed: 05/12/2023

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 04/06/2023.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/ttran/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/066,420	12/15/2022		1480	INH-014US	23	1

CONFIRMATION NO. 1909

UPDATED FILING RECEIPT

51414
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

OC00000056982503

Date Mailed: 05/12/2023

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Ronnie M. Russell, Philadelphia, PA;
Philip R. Johnson, Philadelphia, PA;
James I. Andorko, Philadelphia, PA;
Mohit Sachdeva, Philadelphia, PA;
Bruce Schnepp, Havertown, PA;
Michael Marinelli, Philadelphia, PA;
Jeffrey Foss, Philadelphia, PA;
Debasish Boral, Philadelphia, PA;

Applicant(s)

INTERIUS BIOTHERAPEUTICS, INC., Philadelphia, PA;

Power of Attorney: The patent practitioners associated with Customer Number 051414

Domestic Priority data as claimed by applicant

This appln claims benefit of 63/289,888 12/15/2021
and claims benefit of 63/289,977 12/15/2021
and claims benefit of 63/266,044 12/27/2021
and claims benefit of 63/267,039 01/21/2022

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 03/23/2023
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/066,420**
Projected Publication Date: 08/17/2023
Non-Publication Request: No
Early Publication Request: No
**** SMALL ENTITY ****
Title

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor

community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 18/066,420

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	80		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	350		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	400		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	23 minus 20 =	* 3	x 50 =	350	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	1 minus 3 =	*	x =	0		x =	
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			420			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))			x =	0		x =	
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	1250		TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	*	=			OR		
	Independent (37 CFR 1.16(h))	*	Minus	*	=	x =	x =	OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	*	=	x =	x =	OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	*	=	x =	x =	OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

51414 7590 06/05/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
06/05/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

JGoodwin@goodwinlaw.com
PSousa-Atwood@goodwinlaw.com
US-PatentBos@goodwinlaw.com

Decision Granting Request for Prioritized Examination (Track I)	**Application No.** 18/066,420	**Applicant(s)** Russell et al.	
	Examiner APRIL M WISE	**Art Unit** OPET	**AIA (FITF) Status** Yes

1. THE REQUEST FILED 15 December 2022 IS **GRANTED** .

The above-identified application has met the requirements for prioritized examination

A. ☑ for an original nonprovisional application (Track I).
B. ☐ for an application undergoing continued examination (RCE).

2. **The above-identified application will undergo prioritized examination**. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:

A. filing a **petition for extension of time** to extend the time period for filing a reply;

B. filing an **amendment to amend the application to contain more than four independent claims, more than thirty total claims** , or a multiple dependent claim;

C. filing a **request for continued examination** ;

D. filing a notice of appeal;

E. filing a request for suspension of action;

F. mailing of a notice of allowance;

G. mailing of a final Office action;

H. completion of examination as defined in 37 CFR 41.102; or

I. abandonment of the application.

Telephone inquiries with regard to this decision should be directed to undersigned at (571)272-1642.

In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.

/APRIL M WISE/ Paralegal Specialist, Office of Petitions	

U.S. Patent and Trademark Office
PTO-2298 (Rev. 02-2012)

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

51414 7590 06/23/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
06/23/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

JGoodwin@goodwinlaw.com
PSousa-Atwood@goodwinlaw.com
US-PatentBos@goodwinlaw.com

Office Action Summary	Application No. 18/066,420	Applicant(s) Russell et al.	
	Examiner MICHAEL D BURKHART	Art Unit 1633	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 71-93 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 71-75,78-80 and 86-93 is/are rejected.

8) ☑ Claim(s) 71-93 is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date 1/30/23.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Objections

Claims 71-93 are objected to because of the following informalities: the claims recite, or depend upon claims that recite, a polypeptide that "...comprises a mutation that corresponds to a mutation at position 182...". This is grammatically clumsy and potentially confusing, primarily due to the duplicative use of the term "mutation" in the relevant phrase wherein a single use of the term would suffice. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van*

Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The filing of a terminal disclaimer by itself is not a complete reply to a nonstatutory double patenting (NSDP) rejection. A complete reply requires that the terminal disclaimer be accompanied by a reply requesting reconsideration of the prior Office action. Even where the NSDP rejection is provisional the reply must be complete. See MPEP § 804, subsection I.B.1. For a reply to a non-final Office action, see 37 CFR 1.111(a). For a reply to final Office action, see 37 CFR 1.113(c). A request for reconsideration while not provided for in 37 CFR 1.113(c) may be filed after final for consideration. See MPEP §§ 706.07(e) and 714.13.

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The actual filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-

processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/apply/applying-online/eterminal-disclaimer.

Claims 71-75, 78-80, 86-93 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 71-78, 82-89 of copending Application No. 18/157,421 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the '421 claims recite a polypeptide of the same sequence as the instant claims and comprising a specific alanine substitution at position 182.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL D BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached M-F 8-5.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Babic can be reached on 571 272-8507. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL D BURKHART/
Primary Examiner, Art Unit 1633

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/066,420	Russell et al.
	Examiner	Art Unit
	MICHAEL D BURKHART	1633

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name search (OC search, USPat, USPgPub, EPO, JPO, Derwent) keyword search (OC search, Google)	06/16/2023	MB
STIC search SEQ ID Nos	06/16/2023	MB

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	50	ronnie near2 russell.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 12:45 AM
L2	606	philip near2 johnson.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:19 AM
L3	6	james near2 andorko.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:19 AM
L4	1	mohit near2 sachdeva.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:20 AM
L5	10	bruce near2 schnepp.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:20 AM
L6	31	michael near2 marinelli.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:21 AM
L7	6	jeffrey near2 foss.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:21 AM
L8	0	debasish near2 boral.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:22 AM
L10	25913468	(vsvg OR vsv-g OR (vesicular ADJ stomatitis ADJ virus)) NEAR 5 (envelope OR SU OR surface)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:26 AM
L11	0	L10 WITH (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:27 AM
L12	0	L10 SAME (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:27 AM
L13	633	L10 AND (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:27 AM
L14	14	L10 AND (i182e OR l198e)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:28 AM
L15	9	L10 AND (i182d OR l198d)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:29 AM
L16	28	L10 AND (i182a OR l198a)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:29 AM
L17	344	L10 AND (i182 OR l198)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/06/17 01:29 AM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	18066420
Filing Date	2022-12-15
First Named Inventor	Ronnie M. Russell
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	148165.001401

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4439196	A	1984-03-27	Higuchi	
	1	4447224	A	1984-05-08	DeCant, Jr. et al.	
	1	4447224	A	1984-05-08	Mayfield	
	1	4439196	A	1984-03-27	Higuchi	
	1	4596556	A	1984-05-08	Morrow et al.	
	1	4590556	A	1988-12-13	Morrow et al.	
	1	4816567	A	1984-03-27	Cabilly et al.	
	1	4596556	A	1988-12-13	Burns	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

	9	4946778	A	1990-08-07	Ladner et al.	
	10	5064413	A	1991-11-12	McKinnon et al.	
	10	5064413	A	1991-11-12	Ladner et al.	
	10	5312335	A	1994-05-17	McKinnon et al.	
	10	5064413	A	1995-01-24	McKinnon et al.	
	10	5064413	A	1995-01-24	Peterson et al.	
	10	6004413	A	1999-12-21	Casterman et al.	
	10	6096002	A	2000-08-01	Landau	
	9	6640778	A	2003-09-16	Weston et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

	1	20200216502	A1	2020-07-09	Albertini et al.			

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	0404097	EP	B1	1990-12-27	Behringwerke AG		
	1	1988001649	WO	B1	1988-03-10	Genex Corp.		
	1	1993011161	WO	B1	1988-03-10	Enzon, Inc.		
	1	1988001649	WO	B1	1990-12-27	Casterman		
	1	1994025591	WO	B1	1994-11-10	Unilever PLC		
	1	1988001649	WO	A2	2004-05-21	Ablynx N.V.		
	1	2016065323	WO	A2	2016-04-28	Singh Biotechnology, LLC		
	1	2022183072	WO	B1	2022-09-01	Kelonia Therapeutics, Inc.		

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

EFS Web 2.1.18

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

NON-PATENT LITERATURE DOCUMENTS			Remove
Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	Albertini et al., "Molecular and Cellular Aspects of Rhabdovirus Entry," Viruses (2012) 4:117-129.	
	1	Baert et al., "Influence of Immunogenicity on the Long-Term Efficacy of Infliximab in Crohn's Disease," (2003) New Engl. J. Med. 348:601-608.	
	1	Beniaminovitz et al., "Prevention of Rejection in Cardiac Transplantation by Blockade of the Interleukin-2 Receptor with a Monoclonal Antibody," (2000) New Engl. J. Med. 342(9):613-619.	
	1	Chothia et al., "Canonical Structures for the Hypervariable Regions of Immunoglobulins," (1987) J. Mol. Biol. 196:901-917.	
	1	Chothia et al., "Conformations of Immunoglobulin Hypervariable Regions," (1989) Nature 342: 877-883.	
	6	Clackson et al., "Making Antibody Fragments Using Phage Display Libraries," (1991) Nature 352:624-628. (Abstract Only)	
	1	Finkelshtein et al., "LDL Receptor and its Family Members Serve as the Cellular Receptors for Vesicular Stomatitis Virus," PNAS (2013) 110(18): 7306-7311.	
	1	Ghosh et al., "Natalizumab for Active Crohn's Disease," (2003) New Engl. J. Med. 348:24-32.	
	1	Herold et al., "Anti-CD3 Monoclonal Antibody in New-Onset Type 1 Diabetes Mellitus," (2002) New Engl. J. Med. 346 (22):1692-1698.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

	10	Holliger et al., "Diabodies: Small Bivalent and Bispecific Antibody Fragments," (1993) Proc. Natl. Acad. Sci. USA 90: 6444-6448.	
	10	Holliger et al., "Engineered Antibody Fragments and the Rise of Single Domains," (2005) Nat. Biotechnol. 23(9): 1126-1136.	
	10	Hwang et al., "Engineering a Serum-Resistant and Thermostable Vesicular Stomatitis Virus G Glycoprotein for Pseudotyping Retroviral and Lentiviral Vectors," Gene Ther. (Aug. 2013) 20(8):807-815.	
	13	Kabat, "The Structural Basis for Antibody Complementary," Adv. Prot. Chem. (1978) 32:1-75. (Abstract Only)	
	10	Kabat et al., "Unusual Distributions of Amino Acids in Complementarity-Determining (Hypervariable) Segments of Heavy and Light Chains of Immunoglobulins and Their Possible Roles in Specificity of Antibody-Combining Sites," (1977) J. Biol. Chem. 252(19):6609-6616.	
	13	Lathe, "Synthetic Oligonucleotide Probes Deduced from Amino Acid Sequence Data," J. Molec. Biol. (1985) 183:1-12.	
	13	Lee et al., "ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells," Biol. Blood Marrow Transplant (2019) 25:625-638.	
	13	Lipsky et al., "Infliximab and Methotrexate in the Treatment of Rheumatoid Arthritis," (2000) New Engl. J. Med. 343 (22):1594-1602.	
	10	Liu et al., "Chimeric Mouse-Human IgG1 Antibody that can Mediate Lysis of Cancer Cells," Proc Natl. Acad. Sci., USA (1987) 84:3439-3443.	
	13	Liu et al., "Production of a Mouse-Human Chimeric Monoclonal Antibody to CD20 with Potent Fc-Dependent Biologic Activity," J. Immunology (1987) 139(10):3521-3526.	
	10	Liu et al., "Randomised, Double Blind, Placebo Controlled Study of Interferon Beta-1a in Relapsing-Remitting Multiple Sclerosis Analysed by Area under Disability/Time Curves," J. Neurol. Neurosurg. Psych. (1999) 67:451-456.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

	21	Marks et al., "By-Passing Immunization," J. Mol. Biol. (1991) 222: 581-597.
	22	Milgrom et al., "Treatment of Allergic Asthma with Monoclonal Anti-IgE Antibody," New Engl. J. Med. (1999) 341:1966-1973.
	22	Muller, "[43] Determination of Affinity and Specificity of Anti-Hapten Antibodies by Competitive Radioimmunoassay," Meth. Enzymol. (1983) 92:589-601. (Abstract Only)
	24	Muyldermans et al., "Recognition of Antigens by Single-Domain Antibody Fragments: the Superfluous Luxury of Paired Domains," (2001) Trends Biochem. Sci. 26(4):230-235.
	22	Neelapu et al., "Chimeric Antigen Receptor T-Cell Therapy – Assessment and Management of Toxicities," Nat. Rev. Clin. Oncology (Jan. 2018) 15(1):47-62.
	22	Nikolic et al., "Structural Basis for the Recognition of LDL-Receptor Family Members by VSV Glycoprotein," Nature Comm. (2018) 9(1029):1-12.
	22	Pluckthun, "Antibodies from Escherichia Coli," Nature (4 October 1990) Vol. 347, No. 6292, pgs. 497-498.
	22	Portielji et al., "IL-12: A Promising Adjuvant for Cancer Vaccination," Cancer Immunol. Immunother. (2003) 52:133-144.
	21	Presta, "Selection, Design, and Engineering of Therapeutic Antibodies," J. Allergy Clin. Immunol. (2005) 116 (4):731-736.
	30	Reichmann et al., "Reshaping Human Antibodies for Therapy," Nature (1988) 332(6162):323-327.
	30	Roche et al., "Crystal Structure of the Low-pH Form of the Vesicular Stomatitis Virus Glycoprotein G," Science (14 July 2006) 313:187-191.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

	32	Roche et al., "Structure of the Prefusion Form of the Vesicular Stomatitis Virus Glycoprotein G," Science (9 Feb. 2007) 315:843-848.
	32	Slamon et al., "Use of Chemotherapy Plus a Monoclonal Antibody against HER2 for Metastatic Breast Cancer that Overexpresses HER2," (2001) New Engl. J. Med. 344(11):783-792.
	34	Teachey et al., "Identification of Predictive Biomarkers for Cytokine Release Syndrome after Chimeric Antigen Receptor T-cell Therapy for Acute Lymphoblastic Leukemia," Cancer Discov. (June 2016) 6(6):664-679.
	35	Tsurushita et al., "Humanization of a Chicken Anti-IL-12 Monoclonal Antibody," J. Immuno. Methods (2004) Vol. 295, pgs. 9-19.
	34	Yang et al., "A Randomized Trial of Bevacizumab, an Anti-Vascular Endothelial Growth Factor Antibody, for Metastatic Renal Cancer," (2003) New Engl. J. Med. 349(5):427-434.

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/MICHAEL D BURKHART/	Date Considered	06/17/2023

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	148165.001401

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Christopher R. Bodle/	Date (YYYY-MM-DD)	2023-01-30
Name/Print	Christopher R. Bodle	Registration Number	80,876

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**06/28/2023 04:13:57 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Julianne Holland
PATENT CENTER #	62352719	FILING DATE	12/15/2022
CUSTOMER #	51414	FIRST NAMED INVENTOR	Ronnie M. Russell
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Christopher Bodle

Documents

TOTAL DOCUMENTS: 7

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed.pdf		7	-	38 KB
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed-A....pdf	(1-1)	1	Amendment/Request for Reconsideration-After Non-Final Rejection	16 KB
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed-CLM.pdf	(2-5)	4	Claims	24 KB
INH-014US_Response-to-Non-Final-Office-Action-dtd	(6-7)	2	Applicant Arguments/Remarks Made in an Amendment	22 KB

23-06-23-as-filed-REM.pdf			
FOR_INH-014US_cited_art_from_ISR_WO2020223240A1.pdf	82	Foreign Reference	9958 KB
NPL_INH-014WO_ISR-Written-Opinion_dated_2023-06-15.pdf	14	Non Patent Literature	6755 KB
INH-014US_IDS-SB08-as-filed.pdf	4	Information Disclosure Statement (IDS) Form (SB08)	1234 KB
INH-014US_IDS-Transmittal_Letter-as-filed.pdf	2	Transmittal Letter	21 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed.pdf	D68DC6E6B59465B0F0819AF9321F7357F4C38ABA5E73D7BDAA1FC1F40BE94BECA1376021CC7F249C79251C6A2A5EBB24A56945DDA45BD40C8E266282D86C9FE9
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed-A....pdf	4FECFE038C0F1C6F2500031AD6FA1FD0FF3908D9EAA8F827DD22ECCBBB34F7959F06064545409584A6EAAE942ED7356D400F56D439669464DF2A1CE32D33B801
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed-CLM.pdf	62431F7A3FDB561CE87E0D0F8B3AB6E1B7E0DB2D1C57AE2B685879B90C8F84024EBF7A009710F8B22975BE0DCFF2D0402ED25C7CD399CC8DD182F0B9597A309D
INH-014US_Response-to-Non-Final-Office-Action-dtd 23-06-23-as-filed-REM.pdf	6DDAC72B46CC1FD86E19962D40C10AEF8907FB2AEFBF223381D652D96A98833715E38CAB40F6D6C92E958AAB4FB7739D190BA08FB11870F180AC5021B9EE08A6
FOR_INH-014US_cited_art_from_ISR_W	FF6523F25BD86A0E489C0E15A87F4C175C25180224732EF3F78706F1144A75323A52DDEA55BD4C46B27A71D9A813D8CE0EF

O2020223240A1.pdf	E3E8399DFEC6C14A02A3CF08F2145
NPL_INH-014WO_ISR-Written-Opinion_dated_2023-06-15.pdf	80CBF54619408C365FC4F8601C511312B699E0E73CE471BFB E6F3EC540F4735F80C1E61B1945D08A05810CECF6EF641E86 3E14FD0DB27CDFF8C616757B71FC37
INH-014US_IDS-SB08-as-filed.pdf	31CE0118CC5000CBBBFCE99C1089B85CB6FEAD613D507CE1 6ED2AB39A3BF36D355EB291CD08AEA5265A66ACB6DCCB236 EDA2FE1C61E6C97E3CA56203F3381A89
INH-014US_IDS-Transmittal_Letter-as-filed.pdf	609A86D97B791FFEB8EE3FCC00191A4085066A1F6A74634EE FE1B0CF0800F91B93D5CA51359D9618979EBA7A23D0C06F88 19F661E4177C369E07547AFDCD1091

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: CHRISTOPHER BODLE
UNION TRUST BUILDING
501 GRANT STREET, SUITE 300
PITTSBURGH, PA 15219

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 148165-001402	Date of mailing *(day/month/year)* JUN 15 2023 **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US2022/081616	International filing date *(day/month/year)* 15 December 2022
Applicant INTERIUS BIOTHERAPEUTICS, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   How? Directly to the International Bureau preferably through ePCT, or on paper to:
   The International Bureau of WIPO, 34, chemin des Colombettes, 1211 Geneva 20, Switzerland
   (Facsimile No.: +41 22 338 82 70)

   For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 – 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to any protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.
   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

   Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

   Within 22 months from the priority date, the applicant may request that a supplementary international search be carried out by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Taina Matos Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/220 (revised January 2019)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION
148185-001402	see Form PCT/ISA/220 as well as, where applicable, item 5 below.

International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2022/081616	15 December 2022	16 December 2021

Applicant
INTERIUS BIOTHERAPEUTICS, INC.

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (see Box No. II).

3. ☒ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the drawings to be published with the abstract is Figure No. 2A

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/081616

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☒ forming part of the international application as filed.

   b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/081616

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 63, 64
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 63 and 64 are held as omnibus claims as they refer to an invention "such as those provided for herein."

3. ☒ Claims Nos.: 4-22, 26, 28-61, 65, 69, 70
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/081618

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - INV. - C07K 14/145; A61K 47/68; A61P 35/00; C12N 15/867 (2023.01)
ADD. - A61K 38/16; C12N 5/10; C12N 15/113 (2023.01)

CPC - INV. - C07K 14/145; A61K 47/6835; A61P 35/00; C12N 15/867 (2023.05)
ADD. - A61K 38/162; C12N 5/10; C12N 15/113; C12N 2760/20222
C12N 2760/20223 (2023.05)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic database consulted during the international search (name of database and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2020/223240 A1 (THE BROAD INSTITUTE INC. et al) 05 November 2020 (05.11.2020) entire document	1-3
A	US 2006/0227736 A1 (CHEN et al) 12 September 2006 (12.09.2006) entire document	1-3
A	US 2020/0371088 A1 (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) 26 November 2020 (26.11.2020) entire document	1-3
A	US 2021/0106632 A1 (TANDEM CO. LTD.) 15 April 2021 (15.04.2021) entire document	1-3
A	US 2018/0371064 A1 (UNIVERSITÉ CLAUDE BERNARD LYON 1 et al) 27 December 2018 (27.12.2018) entire document	1-3
A	US 2019/0055568 A1 (UCL BUSINESS PLC) 21 February 2019 (21.02.2019) entire document	1-3

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
01 May 2023	JUN 15 2023
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Taina Matos Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2022)

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-3, 23-25, and 27 are drawn to VSV-G polypeptides.

Group II+: claims 62 and 66-68 are drawn to viral particles, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith.

The first invention of Group I+ is restricted to a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising one mutation selected to be I182D. It is believed that claims 1-3 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

The first invention of Group II+ is restricted to a viral particle comprising a targeting moiety that binds to CD7, comprising a heavy chain with SEQ ID NO: 51, comprising a variable domain with SEQ ID NO: 47, comprising a CDR1 with SEQ ID NO: 35; a CDR2 with SEQ ID NO: 36; and a CDR3 with SEQ ID NO: 37; and a light chain with SEQ ID NO: 52, comprising a variable domain with SEQ ID NO: 48, comprising a CDR1 with SEQ ID NO: 38, a CDR2 with SEQ ID NO: 39, and a CDR3 with SEQ ID NO: 40, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith.

Applicant is invited to elect additional VSV-G polypeptide(s) and/or viral particle(s) comprising a targeting moiety for each additional embodiment, and their respective, corresponding, SEQ ID NOs to be searched in a specific combination by paying an additional fee for each set of election. Each additional elected embodiment requires the selection of a single definition for each viral particle and targeting moiety. An exemplary election would be a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising two mutations selected to be I182D and T214N. Additional VSV-G polypeptide(s) and/or viral particle(s) comprising a targeting moiety for each additional embodiment, and their respective, corresponding, SEQ ID NOs will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the " +" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ and II+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I+, VSV-G polypeptides, are not present in Group II+; and the special technical features of Group II+, viral particles, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith, are not present in Group I+.

The Groups I+ and II+ formulas do not share a significant structural element, requiring the selection of alternative VSV-G polypeptides where " VSV-G polypeptide comprising a mutation that corresponds to a mutation at position 182 of SEQ ID NO: 2" and " VSV-G polypeptide comprising a substitution at positions 1182 and at least one of T214, and T352 of SEQ ID NO: 2," and alternative viral particles comprising a targeting moiety where " viral particle comprising a targeting moiety that binds to CD7 or CD8, or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety that binds to CD7 comprises: a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing; a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37; a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39, and LCDR3 as set forth in SEQ ID NO: 40; a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCDZ as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40; a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48; a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48; a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48; a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51; or a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52; or ii) the targeting moiety that binds to CD8 comprises: a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 56; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 58; the light

chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 59, and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing; a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57; a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60; a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69; or a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70."

Additionally, even if Groups I+ and II+ were considered to share the technical features of a VSV-G polypeptide comprising a mutation; a viral glycoprotein; and a viral particle comprising a targeting moiety, or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety comprises: a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences; and a method of delivering a heterologous molecule to a target cell or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector comprising a targeting moiety that specifically binds to the target cell and a nucleic acid molecule encoding the heterologous molecule; and cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety, these shared technical features do not represent a contribution over the prior art, as disclosed by US 2021/0186632 to Tandem Co., Ltd. (hereinafter, " Tandem") and US 2008/0227736 to Chen et al. (hereinafter, "Chen").

Specifically, Tandem teaches a VSV-G polypeptide comprising a mutation (Abstract, a VSV-G mutated protein).

Further, Chen teaches a viral glycoprotein (Sindbis virus is a member of the Alphavirus genus... the plus-stranded RNA viral genome is complexed with a capsid protein ... surrounded by a lipid bilayer embedded with two integral membrane glycoproteins, Para. [0006]); and a viral particle comprising a targeting moiety (targeted lentiviral vectors that are pseudotyped with mutated Sindbis envelopes, Para. [0010]; a targeting moiety linked to the Sindbis envelope, Para. [0013]; the targeting moiety is an antibody, Para. [0015]), or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety comprises: a polypeptide (the targeting moiety is an antibody, Para. [0015]) comprising: (i) a heavy chain variable region (an exemplary immunoglobulin [antibody] structural unit comprises a tetramer ... composed of two identical pairs of polypeptide chains, each pair having one "light" ... and one "heavy" chain, Para. [0051]) comprising heavy chain CDR1, CDR2, and CDR3 sequences (CDR sequences, Para. [0054]); and (ii) a light chain variable region (an exemplary immunoglobulin [antibody] structural unit comprises a tetramer ... composed of two identical pairs of polypeptide chains, each pair having one "light" ... and one "heavy" chain, Para. [0051]) comprising light chain CDR1, CDR2, and CDR3 sequences (CDR sequences, Para. [0054]); and a method of delivering a heterologous molecule to a target cell (method of gene delivery, Para. [0076]; the pseudotyped targeted lentiviral vectors ... are used to transduce heterologous genes into a cell, Para. [0010]) or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector (a method of gene delivery... intravenous administration, Para. [0076]; the pseudotyped targeted lentiviral vectors ... are used to transduce heterologous genes into a cell, Para. [0010]) comprising a targeting moiety that specifically binds to the target cell and a nucleic acid molecule encoding the heterologous molecule (targeted lentiviral vectors that are pseudotyped with mutated Sindbis envelopes, Para. [0010]; a targeting moiety linked to the Sindbis envelope, Para. [0013]; the targeting moiety is an antibody, Para. [0015]; transduce heterologous genes into a cell, Para. [0010]); and cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety (for preparation of antibodies ... the genes encoding the heavy and light chains of an antibody ... can be cloned from a cell ... and used to produce a recombinant monoclonal antibody, Para. [0053], packing cells ... transiently transfecting cells with plasmids encoding the components of the vector, Para. [0086]).

The inventions listed in Groups I+ and II+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: CHRISTOPHER BODLE
UNION TRUST BUILDING
501 GRANT STREET, SUITE 300
PITTSBURGH, PA 15219

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	JUN 15 2023
Applicant's or agent's file reference	FOR FURTHER ACTION
148165-001402	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2022/081616	15 December 2022	15 December 2021

International Patent Classification (IPC) or both national classification and IPC

IPC(8) - INV. - C07K 14/145; A61K 47/68; A61P 35/00; C12N 15/867 (2023.01)
ADD. - A61K 38/16; C12N 5/10; C12N 15/113 (2023.01)

CPC - INV. - C07K 14/145; A61K 47/6835; A61P 35/00; C12N 15/867 (2023.05)
ADD. - A61K 38/162; C12N 5/10; C12N 15/113; C12N 2760/20222
C12N 2760/20223 (2023.05)

Applicant INTERIUS BIOTHERAPEUTICS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	01 May 2023	Taina Matos PCT Helpdesk: 571-272-4300 Telephone No. 571-272-4300

Form PCT/ISA/237 (cover sheet) (July 2022)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2022/081618

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).

3. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established on the basis of a sequence listing.

a. ☒ forming part of the international application as filed.

b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),

☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2022/081616

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 4-70

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 4-22, 26, 28-61, 63-65, 69, 70 are so unclear that no meaningful opinion could be formed *(specify)*:

Claims 4-22, 26, 28-61, 65, 69, and 70 are multiple dependent claims not drafted in accordance with the second and third sentences of Rule 6.4(a).

Claims 63 and 64 are held as omnibus claims as they refer to an invention "such as those provided for herein."

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 4-70

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing complying with WIPO Standard ST.26, and such listing was not available to the International Searching Authority in the form, language and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a).

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2022/081816

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:

   ☐ paid additional fees.

   ☐ paid additional fees under protest and, where applicable, the protest fee.

   ☐ paid additional fees under protest but the applicable protest fee was not paid.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

<See Supplemental Box>

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-3

Form PCT/ISA/237 (Box No. IV) (July 2022)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2022/081616

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-3	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-3	YES
	Claims	None	NO
Industrial applicability (IA)	Claims	1-3	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-3 have been analyzed subject to the restriction that the claims read on a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising one mutation selected to be I182D.

Claims 1-3 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest:

Regarding claim 1, the prior art of record, individually or in combination, does not teach or fairly suggest a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising one mutation selected to be I182D.

Claims 2 and 3 depend from claim 1, and therefore meet the criteria set out in PCT Article 33(2)-(3) for at least the same reasons as claim 1.

The following prior art is made of record to support and further define the reasons claim 1 meets the criteria set out in PCT Article 33(2)-(3):

(i)US 2019/0055568 to UCL Business PLC (hereinafter, "UCL") teaches a VSV-G protein with 100% sequence identity to instant SEQ ID NO: 2 further comprising a variant(The retroviral env protein may comprise a variant of SEQ ID NO: 10 which retains ability to provide a functional env protein ... VSVG env amino acid sequence SEQ ID NO: 10, Paras. [0103]-[0104]; SEQ ID NO: 10 of UCL comprises a sequence with 100% sequence identity to instant SEQ ID NO: 2).

None of the prior art taken alone or in combination fairly teach or suggest a VSV-G protein with 100% sequence identity to instant SEQ ID NO: 2 further comprising an I182D mutation, as recited above.

Claims 1-3 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2022/081616

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
<Box No. IV Lack of unity of invention>

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-3, 23-25, and 27 are drawn to VSV-G polypeptides.

Group II+: claims 62 and 66-68 are drawn to viral particles, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith.

The first invention of Group I+ is restricted to a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising one mutation selected to be I182Q. It is believed that claims 1-3 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

The first invention of Group II+ is restricted to a viral particle comprising a targeting moiety that binds to CD7, comprising a heavy chain with SEQ ID NO: 51, comprising a variable domain with SEQ ID NO: 47, comprising a CDR1 with SEQ ID NO: 35, a CDR2 with SEQ ID NO: 36, and a CDR3 with SEQ ID NO: 37; and a light chain with SEQ ID NO: 52, comprising a variable domain with SEQ ID NO: 48, comprising a CDR1 with SEQ ID NO: 38, a CDR2 with SEQ ID NO: 39, and a CDR3 with SEQ ID NO: 40, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith.

Applicant is invited to elect additional VSV-G polypeptide(s) and/or viral particle(s) comprising a targeting moiety for each additional embodiment, and their respective, corresponding, SEQ ID NOs to be searched in a specific combination by paying an additional fee for each set of election. Each additional elected embodiment requires the selection of a single definition for each viral particle and targeting moiety. An exemplary election would be a VSV-G polypeptide selected to be SEQ ID NO: 2 comprising two mutations selected to be I182Q and T214N. Additional VSV-G polypeptide(s) and/or viral particle(s) comprising a targeting moiety for each additional embodiment, and their respective, corresponding, SEQ ID NOs will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the " +" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ and II+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I+, VSV-G polypeptides, are not present in Group II+; and the special technical features of Group II+, viral particles, methods of delivering a heterologous molecule to a CD7+ or CD8+ target cell, or methods of treating cancer in a subject associated therewith, and a cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety and a viral glycoprotein associated therewith, are not present in Group I+.

The Groups I+ and II+ formulae do not share a significant structural element, requiring the selection of alternative VSV-G polypeptides where " VSV-G polypeptide comprising a mutation that corresponds to a mutation at position 182 of SEQ ID NO: 2" and " VSV-G polypeptide comprising a substitution at positions 1182 and at least one of T214, and T352 of SEQ ID NO: 2," and alternative viral particles comprising a targeting moiety where " viral particle comprising a targeting moiety that binds to CD7 or CD8, or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety that binds to CD7 comprises: a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 35; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 36; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 37, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 38, the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 39; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 40; or variants of any of the foregoing; a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 47, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; and HCDR3 as set forth in SEQ ID NO: 37; a light chain comprising: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 38; LCDR2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40; a polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 35; HCDR2 as set forth in SEQ ID NO: 36; HCDR3 as set forth in SEQ ID NO: 37; LCDR1 as set forth in SEQ ID NO: 38; LCD2 as set forth in SEQ ID NO: 39; and LCDR3 as set forth in SEQ ID NO: 40; a light chain and a heavy chain, wherein the light chain and a heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 48; a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 48; a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 47; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 48, a heavy chain variable region comprising SEQ ID NO: 47, and a light chain variable region comprising SEQ ID NO: 48; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, at least 95% sequence identity to SEQ ID NO: 51, at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51; or a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 52, having at least 95% sequence identity to SEQ ID NO: 52, having at least 99% sequence identity to SEQ ID NO: 52, or a sequence as set forth in SEQ ID NO: 52; or ii) the targeting moiety that binds to CD8 comprises: a polypeptide that comprises: a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 55;

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 58; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 57, or variants of any of the foregoing; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 56; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 58; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 60; or variants of any of the foregoing; a heavy chain that comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 67, wherein the polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; and HCDR3 as set forth in SEQ ID NO: 57; a light chain that comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 68, wherein the polypeptide maintains the sequences of LCDR1 as set forth in SEQ ID NO: 58; LCDR2 as set forth in SEQ ID NO: 59; and LCDR3 as set forth in SEQ ID NO: 60; a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO. 68, wherein polypeptide maintains the sequences of HCDR1 as set forth in SEQ ID NO: 55; HCDR2 as set forth in SEQ ID NO: 56; HCDR3 as set forth in SEQ ID NO: 57; LCDR1 as set forth in SEQ ID NO: 58; LCD2 as set forth in SEQ ID NO' 59, and LCDR3 as set forth in SEQ ID NO: 60; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 67; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 68; a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain variable region comprises SEQ ID NO: 67, and the light chain variable region comprises SEQ ID NO: 68; a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 69, at least 95% sequence identity to SEQ ID NO: 69, at least 99% sequence identity to SEQ ID NO: 69, or a sequence as set forth in SEQ ID NO: 69; or a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 70, having at least 95% sequence identity to SEQ ID NO: 70, having at least 99% sequence identity to SEQ ID NO: 70, or a sequence as set forth in SEQ ID NO: 70."

Additionally, even if Groups I- and II- were considered to share the technical features of a VSV-G polypeptide comprising a mutation; a viral glycoprotein; and a viral particle comprising a targeting moiety, or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety comprises: a polypeptide comprising: (i) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences; and (ii) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences; and a method of delivering a heterologous molecule to a target cell or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector comprising a targeting moiety that specifically binds to the target cell and a nucleic acid molecule encoding the heterologous molecule; and cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety, these shared technical features do not represent a contribution over the prior art, as disclosed by US 2021/0190632 to Tandem Co., Ltd. (hereinafter, " Tandem") and US 2008/0227736 to Chen et al. (hereinafter, "Chen").

Specifically, Tandem teaches a VSV-G polypeptide comprising a mutation (Abstract, a VSV-G mutated protein).

Further, Chen teaches a viral glycoprotein (Sindbis virus is a member of the Alphavirus genus... the plus-stranded RNA viral genome is complexed with a capsid protein ... surrounded by a lipid bilayer embedded with two integral membrane glycoproteins, Para. [0006]); and a viral particle comprising a targeting moiety (targeted lentiviral vectors that are pseudotyped with mutated Sindbis envelopes, Para. [0010]; a targeting moiety linked to the Sindbis envelope, Para. [0013]; the targeting moiety is an antibody, Para. [0016]), or a pharmaceutical composition comprising the same, wherein: i) the targeting moiety comprises: a polypeptide (the targeting moiety is an antibody, Para. [0016]) comprising: (i) a heavy chain variable region (an exemplary immunoglobulin [antibody] structural unit comprises a tetramer ... composed of two identical pairs of polypeptide chains, each pair having one "light" ... and one "heavy" chain, Para. [0051]) comprising heavy chain CDR1, CDR2, and CDR3 sequences (CDR sequences, Para. [0054]); and (ii) a light chain variable region (an exemplary immunoglobulin [antibody] structural unit comprises a tetramer ... composed of two identical pairs of polypeptide chains, each pair having one "light" ... and one "heavy" chain, Para. [0051]) comprising light chain CDR1, CDR2, and CDR3 sequences (CDR sequences, Para. [0054]), and a method of delivering a heterologous molecule to a target cell (method of gene delivery, Para. [0076]; the pseudotyped targeted lentiviral vectors ... are used to transduce heterologous genes into a cell, Para. [0010]) or a method of treating cancer in a subject, the method comprising contacting a cell with, or administering to the subject, a pseudotyped viral vector (a method of gene delivery... intravenous administration, Para. [0076]; the pseudotyped targeted lentiviral vectors ... are used to transduce heterologous genes into a cell, Para. [0010]) comprising a targeting moiety that specifically binds to the target cell and a nucleic acid molecule encoding the heterologous molecule (targeted lentiviral vectors that are pseudotyped with mutated Sindbis envelopes, Para. [0010]; a targeting moiety linked to the Sindbis envelope, Para. [0013]; the targeting moiety is an antibody, Para. [0016]; transduce heterologous genes into a cell, Para. [0010]); and cell comprising one or more heterologous nucleic acid molecules encoding for a targeting moiety, wherein the heterologous nucleic acid molecules comprise a nucleic acid sequence encoding for a targeting moiety (for preparation of antibodies ... the genes encoding the heavy and light chains of an antibody ... can be cloned from a cell ... and used to produce a recombinant monoclonal antibody, Para. [0053]; packing cells ... transiently transfecting cells with plasmids encoding the components of the vector, Para. [0086]).

The inventions listed in Groups I- and II- therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	18066420
Filing Date	2022-12-15
First Named Inventor	Ronnie M. Russell
Art Unit	1633
Examiner Name	BURKHART, MICHAEL D
Attorney Docket Number	INH-014US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080227736	A1	2008-09-18	Chen et al.	
	1	20200371088	A1	2020-11-26	Birnbaum et al.	
	1	20210106632	A1	2008-09-18	Chen et al.	
	1	20200371088	A1	2019-02-21	Pulé et al.	
	1	20200371088	A1	2018-12-27	FUSIL et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	1633
	Examiner Name	BURKHART, MICHAEL D
	Attorney Docket Number	INH-014US

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2020223240	WO	A1	2020-11-05	The Broad Institute, Inc		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	International Search Report and Written Opinion for PCT/US2022/081616, dated June 15, 2023, 14 pages.	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	1633
	Examiner Name	BURKHART, MICHAEL D
	Attorney Docket Number	INH-014US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Christopher R. Bodle/	Date (YYYY-MM-DD)	2023-06-28
Name/Print	Christopher R. Bodle	Registration Number	80,876

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Attorney Docket No. INH-014US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	Ronnie M. Russell et al.
Application No.	:	18/066,420
Filed	:	December 15, 2022
Group Art Unit	:	1633
Confirmation No.	:	1909
Examiner	:	Michael D Burkhart

Title: PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO NON FINAL OFFICE ACTION

Dear Commissioner:

This paper is filed in response to the Non Final Office Action dated June 23, 2023. No extensions of time are believed to be necessary, however, if one is necessary, Applicant respectfully requests that one be granted and the appropriate fee be charged against the deposit account indicated herein. Accordingly, this paper is timely filed.

Amendments to the Claims begin on page 2; and
Remarks begin on page 6.

AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions, or listings of the claims in the present application.

1 - 70. (Cancelled)

71 - 75. (Cancelled)

76. (Currently Amended) ~~The~~A polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2 and ~~of claim 1, wherein the mutation at position is~~ a I182E mutation as compared to SEQ ID NO: 2.

77. (Currently Amended) ~~The~~A polypeptide comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 2 and ~~of claim 1, wherein the mutation at position 182 comprises~~ a I182D mutation as compared to SEQ ID NO: 2.

78. (Currently Amended) The polypeptide of claim [[1]]76, wherein the polypeptide further comprises a mutation ~~that corresponds to a mutation~~ at position 214, a mutation at position 352, or a mutation at both position 214 and position 352 as compared to [[of]] SEQ ID NO: 2.

79. (Currently Amended) The polypeptide of claim [[1]]76, wherein the polypeptide further comprises a T214N mutation, a T352A mutation, or a combination thereof, as compared to SEQ ID NO: 2.

80. (Currently Amended) The polypeptide of claim [[1]]76, wherein the polypeptide further comprises a T214N mutation and a T352A mutation as compared to SEQ ID NO: 2.

81. (Currently Amended) The polypeptide of claim [[1]]77, ~~wherein the mutation at position 182 comprises a I182E or I182D mutation as compared to SEQ ID NO: 2 and~~ wherein the polypeptide further comprises a ~~T214N~~ mutation at position 214, a ~~T352A~~ mutation at position

352, or a ~~combination thereof~~mutation at both position 214 and 352, as compared to SEQ ID NO: 2.

82. (Currently Amended) The polypeptide of claim [[1]]77, ~~wherein the mutation at position 182 comprises a I182E mutation as compared to SEQ ID NO: 2 and~~ wherein the polypeptide further comprises a T214N mutation, a T352A mutation, or a combination thereof, as compared to SEQ ID NO: 2.

83. (Currently Amended) The polypeptide of claim [[1]]77, ~~wherein the mutation at position 182 comprises a I182E or I182D mutation as compared to SEQ ID NO: 2 and~~ wherein the polypeptide further comprises a T214N mutation and a T352A mutation as compared to SEQ ID NO: 2.

84. (Cancelled).

85. (Currently Amended) The polypeptide of claim [[1]]76, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 23.

86. (Currently Amended) A nucleic acid molecule encoding the polypeptide of claim [[1]]76.

87. (Previously Presented) A vector comprising the nucleic acid molecule of claim 86.

88. (Previously Presented) A cell comprising the nucleic acid molecule of claim 86.

89. (Currently Amended) A viral particle comprising the polypeptide of claim [[1]]76.

90. (Previously Presented) The viral particle of claim 89, wherein the viral particle is a lentivirus comprising the polypeptide.

91. (Previously Presented) The viral particle of claim 89, wherein the viral particle further comprises a heterologous nucleic acid molecule encoding a heterologous molecule of interest.

92. (Previously Presented) The viral particle of claim 91, wherein the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA, a polypeptide, a viral payload, a viral genome, or a combination thereof.

93. (Previously Presented) The viral particle of claim 91, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR").

94. (New) The polypeptide of claim 76, wherein the polypeptide comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 2.

95. (New) The polypeptide of claim 76, wherein the polypeptide comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 2.

96. (New) The polypeptide of claim 76, wherein the polypeptide comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 2.

97. (New) The polypeptide of claim 76, wherein the polypeptide comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 2.

98. (New) The polypeptide of claim 77, wherein the polypeptide comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 2.

99. (New) The polypeptide of claim 77, wherein the polypeptide comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 2.

100. (New) The polypeptide of claim 77, wherein the polypeptide comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 2.

101. (New) The polypeptide of claim 77, wherein the polypeptide comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 2.

102. (New) The polypeptide of claim 77, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 22.

103. (New) A viral particle comprising the polypeptide of claim 85.

104. (New) The viral particle of claim 103, wherein the viral particle further comprises a nucleic acid molecule encoding a chimeric antigen receptor.

105. (New) A viral particle comprising the polypeptide of claim 102.

106. (New) The viral particle of claim 105, wherein the viral particle further comprises a nucleic acid molecule encoding a chimeric antigen receptor.

REMARKS

Claims 71-93 were pending in the present application. Claims 76-83, 85, 86, and 89 have been amended as shown. Claims 71-75 and 84 have been cancelled without prejudice. New claims 94-106 have been added. Support for claim amendments and new claims can be found throughout the as-filed specification and claims. Upon entry of the present amendment, claims 76-83 and 85-106 will be pending. The pending claims still satisfy the rules of Prioritized Examination regarding the total number of independent claims (no more than 4), total claims (no more than 30) and the prohibition of multiple dependent claims. No new matter has been added.

Claim Objections

Claims 71-93 were objected to because the Office alleges that the recitation of the term "mutation" in the claim twice was "potentially confusing." (Office Action, p. 2). Applicant respectfully disagrees, but solely to advance prosecution, the claims have been amended consistent with the Office's suggestion. Applicant respectfully asserts that the claims are clear and not confusing.

In view of the foregoing, Applicant respectfully requests that the objection to the claims be with withdrawn.

Double Patenting

Claims 71-75, 78-80, and 86-93 have been provisionally rejected on the ground of nonstatutory double patenting over claims 71-78, and 82-89 of copending Application No. 18/157,421. Claims 71-75 have been cancelled herein without prejudice. Claims 78-80 and 86-93 have been amended to depend, either directly or indirectly, on claims 76 and 77, which were rewritten as independent claims. Claims 76 and 77 of the present application were not included in the present rejection. Accordingly, the provisional rejection on the ground of nonstatutory double patenting has been rendered moot.

In view of the foregoing, Applicant respectfully requests that the provisional rejection on the ground of nonstatutory double patenting be withdrawn.

CONCLUSION

In view of the foregoing, Applicant respectfully submits that the claims are in condition for allowance. A notice of allowance is, therefore, earnestly solicited. The Office is invited to contact Applicant's undersigned representative at 445-207-7829 if there are any questions regarding Applicant's presently claimed subject matter.

The Commissioner is hereby authorized to charge any additional fees which may be required for this submission, or credit any overpayment, to Deposit Account No. 07-1700.

Respectfully submitted,
/Christopher R. Bodle /

Christopher R. Bodle, Ph.D.
Registration No. 80,876

GOODWIN PROCTER LLP
1900 N Street, NW
Washington, DC 20036
Telephone 1-445-207-7829
Date: June 28, 2023

Espacenet

Bibliographic data: WO2020223240 (A1) — 2020-11-05

AFFINITY-BASED MULTIPLEXING FOR LIVE-CELL MONITORING OF COMPLEX CELL POPULATIONS

Inventor(s): BORRAJO JACOB [US]; TSAI FUNIEN [US]; BLAINEY PAUL [US]; NAJIA MOHAMAD [US]; LE HONG ANH ANNA [US] ± (BORRAJO, Jacob, ; TSAI, FuNien, ; BLAINEY, Paul, ; NAJIA, Mohamad, ; LE, Hong Anh Anna)

Applicant(s): BROAD INST INC [US]; MASSACHUSETTS INST TECHNOLOGY [US]; BORRAJO JACOB [US]; TSAI FUNIEN [US] ± (THE BROAD INSTITUTE, INC, ; MASSACHUSETTS INSTITUTE OF TECHNOLOGY, ; BORRAJO, Jacob, ; TSAI, FuNien)

Classification: - **international:** ***A61K39/12; A61K39/21; C07K14/005; C07K14/16; C12N15/10; C12N7/04***

- **cooperative:** **A61P35/00 (EP)**; **C07K14/005 (EP, US)**; **C12N15/1072 (EP, US)**; **C12N15/86 (EP, US)**; **C12Q1/6804 (EP)**; **C12Q1/6806 (EP)**; **G01N33/5005 (US)**; **G01N33/5008 (EP)**; C12N2740/13023 (EP, US); C12N2740/13031 (EP, US); C12N2740/16023 (EP, US); C12N2740/16031 (EP, US); C12N2740/16222 (EP, US); C12N2750/14123 (US); C12N2750/14143 (EP) more

Application number: WO2020US30286 20200428 Global Dossier

Priority number(s): US201962840373P 20190429

Also published as: US2022228168 (A1)

Abstract of WO2020223240 (A1)

Compositions and methods for inducing and isolating virus-like particles (VLPs), and for allowing real-time assessment of VLP-captured analytes obtained from targeted living mammalian cells, are provided.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
05 November 2020 (05.11.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/223240 A1

(51) International Patent Classification:
A61K 39/12 (2006.01) *C07K 14/16* (2006.01)
A61K 39/21 (2006.01) *C12N 7/04* (2006.01)
C07K 14/005 (2006.01) *C12N 15/10* (2006.01)

(21) International Application Number:
PCT/US2020/030286

(22) International Filing Date:
28 April 2020 (28.04.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/840,373 29 April 2019 (29.04.2019) US

(71) Applicants: **THE BROAD INSTITUTE, INC.** [US/US]; 415 Main Street, Cambridge, Massachusetts 02142 (US). **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** [US/US]; 77 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US).

(72) Inventors; and
(71) Applicants: **BORRAJO, Jacob** [US/US]; c/o Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **TSAI, FuNien** [US/US]; c/o The Broad Institute, Inc., 415 Main Street, Cambridge, Massachusetts 02142 (US).

(72) Inventors: **BLAINEY, Paul**; c/o The Broad Institute, Inc., 415 Main Street, Cambridge, Massachusetts 02142 (US). **NAJIA, Mohamad**; c/o Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **LE, Hong Anh Anna**; c/o Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US).

(74) Agent: **COWLES, Christopher R.** et al.; Burns & Levinson, LLP, 125 High Street, Boston, Massachusetts 02110 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
--- *with international search report (Art. 21(3))*

(54) **Title:** AFFINITY-BASED MULTIPLEXING FOR LIVE-CELL MONITORING OF COMPLEX CELL POPULATIONS

(57) **Abstract:** Compositions and methods for inducing and isolating virus-like particles (VLPs), and for allowing real-time assessment of VLP-captured analytes obtained from targeted living mammalian cells, are provided.

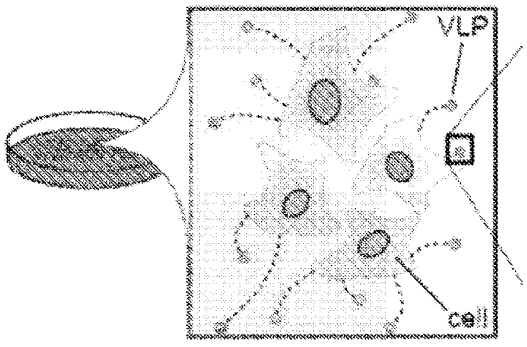


FIG. 1A

WO 2020/223240 A1

AFFINITY-BASED MULTIPLEXING FOR LIVE-CELL MONITORING OF COMPLEX CELL POPULATIONS

CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 62/840,373, filed April 29, 2019, entitled "Affinity-Based Multiplexing for Live-Cell Monitoring of Complex Cell Populations," the entire contents of which are incorporated herein by reference.

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

This invention was made with government support under Grant No. 1DP2HL141005 awarded by the National Institutes of Health. The government has certain rights in the invention.

FIELD OF THE DISCLOSURE

The present disclosure relates to a method for live-cell monitoring of complex cell populations. More particularly, the present disclosure relates to compositions and methods for isolating and analyzing virus-like particles (VLPs) having cell line specific affinity-tagged envelopes.

BACKGROUND OF THE INVENTION

While dramatic throughput advances in sequencing technologies have rendered transcriptome profiling via deep sequencing of even small volumes of cellular samples nearly routine, such methods tend to rely upon cell lysis to obtain samples for sequencing. A need therefore exists for a process that can yield transcriptome information from living cells, thereby allowing for expression profile monitoring of the same population(s) of cells throughout a time course.

BRIEF SUMMARY OF THE INVENTION

The current disclosure relates, at least in part, to the discovery of compositions and methods capable of achieving assessment of living mammalian cell analytes across a time course, *via* induction of targeted virus like particle (VLP) generation in living cells and isolation/analysis of such VLPs to identify VLP-captured mammalian cell analytes.

In one aspect, the instant disclosure provides a mammalian cell harboring a virus like particle (VLP) producing protein and an epitope-tagged viral surface protein.

Another aspect of the instant disclosure provides a mammalian cell harboring an epitope-tagged virus like particle (VLP) producing protein.

An additional aspect of the instant disclosure provides a mammalian cell harboring a virus like particle (VLP) producing protein and a viral surface protein of a virus that differs from the virus of the virus like particle (VLP) producing protein (thereby generating a pseudotyped VLP).

In certain embodiments, the VLP is a non-enveloped virus VLP. Optionally, the non-enveloped virus harbors an engineered affinity tag. Optionally, the non-enveloped virus VLP is of an *Adenoviridae*, a *Papovaviridae*, a *Parvoviridae*, and/or an *Anelloviridae* family virus

In one embodiment, the virus like particle (VLP) producing protein is a retroviral gag protein or a viral gag-like protein. Optionally, the viral gag protein is a murine leukemia virus (MLV) gag protein, a retrovirus matrix protein, a rhabdovirus matrix (M) protein (optionally VSVM protein), a filovirus viral core protein (optionally an Ebola VP40 viral protein), a Rift Valley Fever virus N protein (optionally RVFV N Protein having GenBank serial number NP049344), a coronavirus M, E and/or NP protein (optionally GenBank serial number NP040838 for NP protein, GenBank serial number NP 040835 for M protein, GenBank serial number CAC39303 for E protein of Avian Infections Bronchitis Virus and GenBank serial number NP828854 for E protein of the SARS virus), a bunyavirus N protein (optionally the bunyavirus N protein of GenBank serial number AAA47114), an influenza M1 protein, a paramyxovirus M protein, an arenavirus Z protein (optionally a Lassa Fever Virus Z protein), and/or an AAV gag-like protein (optionally AAV1 capsid, AAV2 capsid, AAV3 capsid, AAV4 capsid, AAV5 capsid, AAV6 capsid, AAV7 capsid, AAV8 capsid, AAV9 capsid, AAV10 capsid, AAV11 capsid, AAV12 capsid, and/or AAV13 capsid), and/or combinations thereof. Optionally, the epitope-tagged viral surface protein is a Vesicular Stomatitis Virus (VSV) glycoprotein (VSV-G) or a mutagenized form of VSV-G. Optionally, the mutagenized form of VSV-G prevents VSV-G-mediated cellular uptake.

In certain embodiments, the epitope-tagged viral surface protein is an epitope-tagged viral envelope protein. Optionally, the epitope-tagged viral envelope protein is an epitope-tagged form of any of the following: a Vesicular Stomatitis Virus (VSV) glycoprotein, a retrovirus glycoprotein (optionally a human immunodeficiency virus (HIV) envelope glycoprotein (optionally HIVSF162 envelope glycoprotein of GenBank serial number M65024)), a simian immunodeficiency virus (SIV) envelope glycoprotein (optionally SIVmac239 envelope glycoprotein of GenBank serial number M33262), a simian-human immunodeficiency virus (SHIV) envelope glycoprotein (optionally SHIV-89.6p envelope

glycoprotein of GenBank serial number U89134), a feline immunodeficiency virus (FIV) envelope glycoprotein (optionally FIV envelope glycoprotein of GenBank serial number L00607), a feline leukemia virus (FLV) envelope glycoprotein (optionally the FLV envelope glycoprotein of GenBank serial number M12500), a bovine immunodeficiency virus (BIV) envelope glycoprotein (optionally the BIV envelope glycoprotein of GenBank serial number NC001413), a bovine leukemia virus (BLV) envelope glycoprotein (optionally of GenBank serial number AF399703), an equine infectious anemia virus envelope glycoprotein (optionally the equine infectious anemia virus envelope glycoprotein of GenBank serial number NC001450), a human T-cell leukemia virus envelope glycoprotein (optionally the human T-cell leukemia virus envelope glycoprotein of GenBank serial number AF0033817), a mouse mammary tumor virus envelope glycoprotein (MMTV), a bunyavirus glycoprotein (optionally a Rift Valley Fever virus (RVFV) glycoprotein (optionally the RVFV envelope glycoprotein of GenBank serial number M11157)), an arenavirus glycoprotein (optionally a Lassa fever virus glycoprotein (optionally of GenBank serial number AF333969))), a filovirus glycoprotein (e.g., an Ebola virus glycoprotein (GenBank serial number NC002549)), a corona virus glycoprotein (optionally of GenBank serial number SARS coronavirus spike protein AAP13567), an influenza virus glycoprotein (optionally of GenBank serial number V01085), a paramyxovirus glycoprotein (optionally of GenBank serial number NC002728 for Nipah virus F and G proteins), a rhabdovirus glycoprotein (optionally of GenBank serial number NP049548)), an alphavirus glycoprotein (optionally of GenBank serial number AAA48370 for Venezuelan equine encephalomyelitis (VEE)), a flavivirus glycoprotein (optionally of GenBank serial number NC001563 for West Nile virus and/or a Hepatitis C Virus glycoprotein), and/or a Herpes Virus glycoprotein (optionally a cytomegalovirus glycoprotein), and/or combinations thereof.

In one embodiment, the epitope-tagged viral surface protein is Coronavirus gpE1, Coronavirus Peplomer Protein E1, Coronavirus Peplomer Protein E2 JHM, Hepatitis Virus (MHV), Glycoprotein E2, LaCrosse Virus Envelope Glycoprotein G1, Simian Sarcoma Virus Glycoprotein 70, Viral Envelope Glycoprotein gp55 (Friend Virus), and/or Viral Envelope Glycoprotein gPr90 (Murine Leukemia Virus).

In some embodiments, the epitope tag of the epitope-tagged viral surface protein is one or more of the following: FLAG (DYKDDDDK; SEQ ID NO: 3), 6 x His (HHHHHH; SEQ ID NO: 4), HA (YPYDVPDYA; SEQ ID NO: 5), c-myc (EQKLISEEDL; SEQ ID NO: 6), V5 tag (GKPIPNPLLGLDST; SEQ ID NO: 7), AU1 tag (DTYRYI; SEQ ID NO: 8), AU5 tag (TDFYLK; SEQ ID NO: 9), Glu-Glu tag (EYMPME; SEQ ID NO: 10), OLLAS

(SGFANELGPRLMGK; SEQ ID NO: 11), T7 tag (MASMTGGQQMG; SEQ ID NO: 12), VSV-G tag (YTDIEMNRLGK; SEQ ID NO: 13), E-Tag (GAPVPYPDPLEPR; SEQ ID NO: 14), S-Tag (KETAAAKFERQHMDS; SEQ ID NO: 15), HSV tag (SQPELAPEDPED; SEQ ID NO: 16), KT3 tag (KPPTPPPEPET; SEQ ID NO: 17), TK15 tag, GST tag, Protein A tag, CD tag, Strep-Tag (WSHPQFEK; SEQ ID NO: 18), MBP tag, CBD tag, Avi tag (CGLNDIFEAQKIEWHE; SEQ ID NO: 19), CBP tag, TAP tag, and/or SF-TAP tag.

In one embodiment, the mammalian cell is infected by a virus. Optionally, the mammalian cell is infected by AAV (and optionally adenovirus, HPV or other virus), or by a retrovirus. Optionally, the retrovirus is a lentivirus.

In some embodiments, the mammalian cell is a cell in culture

In one embodiment, the mammalian cell is a neuronal cell. Optionally, the mammalian cell is a primary cortical neuron. Optionally, the primary cortical neuron is an excitatory neuron or an inhibitory neuron.

In certain embodiments, the mammalian cell is a cell *in vivo*.

In some embodiments, the VLP producing protein and/or the epitope-tagged viral surface protein are produced by the mammalian cell *via* a genomically integrated nucleic acid sequence that encodes for the VLP producing protein and/or the epitope-tagged viral surface protein. Optionally, the nucleic acid sequence that encodes for the VLP producing protein and/or the epitope-tagged viral surface protein is under the control of a mammalian promoter. Optionally, the promoter is a CMV promoter, a SV40 promoter and/or a tissue-specific mammalian promoter. Optionally, the tissue-specific mammalian promoter is a mDlx, CamKII, Syn1, NSE, PDGF and/or Ta1 promoter. Optionally, the tissue-specific mammalian promoter is a CamKII promoter and/or a mDlx promoter.

An additional aspect of the instant disclosure provides a method for obtaining an expression profile of a living cell, the method involving: (a) providing a living cell; (b) introducing a nucleic acid sequence encoding for a VLP producing protein to the living cell, where introduction of the nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cell; (c) isolating VLPs produced by the living cell *via* binding of a VLP protein; and (d) performing RNA sequencing upon the isolated VLPs, thereby obtaining expression profile information for the isolated VLPs, where the expression profile information for the isolated VLPs reflects the expression profile of the living cell, thereby obtaining an expression profile of the living cell.

In certain embodiments, the VLP protein of step (c) is the VLP producing protein. Optionally, the VLP producing protein is tagged. Optionally, the tag is an epitope tag.

In some embodiments, the VLP protein of step (c) is a capsid protein of the VLP or an envelope protein of the VLP.

In another embodiment, the VLP protein of step (c) is a host cell membrane protein. Optionally, the VLP protein of step (c) is an affinity-tagged host cell membrane protein.

In an additional embodiment, the capsid protein of the VLP or the envelope protein of the VLP is tagged. Optionally, the tag is an epitope tag.

In some embodiments, an antibody is used to bind the VLP protein in step (c).

In another embodiment, the antibody binds the VLP producing protein, a capsid protein of the VLP, and/or an envelope protein of the VLP.

Another aspect of the instant disclosure provides a method for obtaining an expression profile of a living cell, the method involving: (a) providing a living cell; (b) introducing a first nucleic acid sequence harboring a nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid harboring a nucleic acid sequence encoding for an epitope-tagged viral surface protein to the living cell, where introduction of the first nucleic acid sequence harboring the nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cell; (c) isolating VLPs produced by the living cell *via* binding of the epitope-tagged viral surface protein; and (d) performing RNA sequencing upon the isolated VLPs, thereby obtaining expression profile information for the isolated VLPs, where the expression profile information for the isolated VLPs reflects the expression profile of the living cell, thereby obtaining an expression profile of the living cell.

In certain embodiments, the living cell is a mammalian cell. Optionally, the living cell is a mammalian cell in culture.

In some embodiments, the living cell is a neuronal cell. Optionally, the neuronal cell is a primary cortical neuron. Optionally, the primary cortical neuron is an excitatory neuron or an inhibitory neuron.

In one embodiment, the living cell is a cell *in vivo*. Optionally, the living cell is a cell in a mouse model of disease. Optionally, the living cell is a cell in an engineered patient-derived xenograft (PDX) model for glioblastoma multiforme (GBM).

In some embodiments, the living cell is a living cell in a rat. Optionally, the living cell is a primary rat cortical neuron or a primary rat hippocampal neuron. Optionally, the living cell is obtained from microsurgically dissected tissue. Optionally the living cell is obtained from an E18 Sprague Dawley rat.

In some embodiments, the first nucleic acid sequence and the second nucleic acid sequence are present on the same nucleic acid construct.

In one embodiment, the first nucleic acid sequence and the second nucleic acid sequence are present on different nucleic acid constructs.

In certain embodiments, the first nucleic acid sequence and/or the second nucleic acid sequence are integrated in the living cell genome.

In one embodiment, the VLP producing protein and/or the epitope-tagged viral surface protein is under the control of a mammalian promoter. Optionally, the mammalian promoter is a CMV promoter, a SV40 promoter and/or a tissue-specific mammalian promoter. Optionally, the tissue-specific mammalian promoter is a CamKII promoter and/or a mDlx promoter.

An additional aspect of the instant disclosure provides a method for obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells, the method involving: (a) providing a first population of living cells; (b) introducing a first nucleic acid sequence harboring a nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid harboring a nucleic acid sequence encoding for a first epitope-tagged viral surface protein to the first population of living cells, where introduction of the first nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the first population of living cells; (c) providing a second population of living cells; (d) introducing the first nucleic acid sequence harboring a nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid harboring a nucleic acid sequence encoding for a second epitope-tagged viral surface protein to the second population of living cells, where introduction of the first nucleic acid sequence comprising a nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the second population of living cells; (e) isolating VLPs produced by the first population of living cells *via* binding of the first epitope-tagged viral surface protein; (f) obtaining a first analyte profile from the isolated VLPs of the first population of living cells; (g) isolating VLPs produced by the second population of living cells *via* binding of the second epitope-tagged viral surface protein; and (h) obtaining a second analyte profile from the isolated VLPs of the second population of living cells, thereby obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells.

In one embodiment, the analyte profile includes transcript information (e.g., transcriptome expression levels).

An additional aspect of the instant disclosure provides a method for obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second

population of living cells, the method involving: (a) providing a first population of living cells; (b) introducing a first nucleic acid sequence encoding for a VLP producing protein to the first population of living cells, where introduction of the first nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the first population of living cells; (c) providing a second population of living cells; (d) introducing a second nucleic acid sequence encoding for a VLP producing protein to the second population of living cells, where introduction of the second nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the second population of living cells; (e) isolating VLPs produced by the first population of living cells *via* binding of a first VLP protein; (f) obtaining a first analyte profile from the isolated VLPs of the first population of living cells; (g) isolating VLPs produced by the second population of living cells *via* binding of a second VLP protein; and (h) obtaining a second analyte profile from the isolated VLPs of the second population of living cells, thereby obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells.

In certain embodiments, the first VLP protein is specific to the first population of cells and the second VLP protein is specific to the second population of cells. Optionally, the first VLP protein is the VLP producing protein encoded by the first nucleic acid and/or the second VLP protein is the VLP producing protein encoded by the second nucleic acid.

In some embodiments, the binding of isolating step (e) is performed using an antibody and/or the binding of isolating step (g) is performed using an antibody.

In another embodiment, the first VLP protein and/or the second VLP protein is tagged. Optionally, the tag is an epitope tag.

An additional aspect of the disclosure provides a method for assessing a test compound for efficacy and/or toxicity in living cells, the method involving: (a) providing a population of living cells; (b) introducing a nucleic acid sequence encoding for a VLP producing protein to the living cells, where introduction of the nucleic acid sequence encoding for the VLP producing protein is sufficient to induce budding of VLPs from the living cells; (c) contacting the living cells with a test compound; (d) isolating VLPs produced by the living cells *via* binding of a VLP protein; and (e) obtaining analyte profile information from the isolated VLPs, where the analyte profile information indicates the efficacy and/or toxicity of the test compound, thereby assessing a test compound for efficacy and/or toxicity in living cells. Another aspect of the instant disclosure provides a method for assessing a test compound for efficacy and/or toxicity in living cells, the method involving: (a) providing a population of living cells; (b) introducing a first nucleic acid sequence harboring a nucleic acid sequence

encoding for a VLP producing protein and a second nucleic acid sequence harboring a nucleic acid sequence encoding for an epitope-tagged viral surface protein to the living cells, where introduction of the nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cells; (c) contacting the living cells with a test compound; (d) isolating VLPs produced by the living cells *via* binding of the epitope-tagged viral surface protein; and (e) obtaining analyte profile information from the isolated VLPs, where the analyte profile information indicates the efficacy and/or toxicity of the test compound, thereby assessing a test compound for efficacy and/or toxicity in living cells.

Definitions

As used herein, the term "virus like particle (VLP) producing protein" refers to any protein capable of prompting a mammalian cell harboring such a VLP producing protein to produce a VLP. In certain aspects, a VLP producing protein can refer to a single, exogenous protein capable of inducing VLP formation (e.g., retroviral gag protein), or a VLP producing protein may act in concert with other VLP producing proteins to achieve VLP formation.

The term "epitope-tagged viral surface protein" as used herein refers to a protein of a virus for which at least a portion of the protein has surface exposure, and to which an epitope tag is attached. In certain aspects an "epitope-tagged viral surface protein" is an epitope tagged viral envelope protein (e.g., VSV-G).

The term "fusion protein" as used herein refers to an engineered polypeptide that combines sequence elements excerpted from two or more other proteins, optionally from two or more naturally-occurring proteins.

The terms "transfect," "transfects," "transfecting" and "transfection" as used herein refer to the delivery of nucleic acids (usually DNA or RNA) to the cytoplasm or nucleus of cells, e.g., through the use of cationic lipid vehicle(s) and/or by means of electroporation, or other art-recognized means of transfection.

The term "transduction," as used herein refers to the delivery of nucleic acids (usually DNA or RNA) to the cytoplasm or nucleus of cells through the use of viral delivery, e.g., *via* lentiviral delivery vectors/plasmids, or other art-recognized means of transduction.

The term "plasmid" as used herein refers to a construction comprised of genetic material designed to direct transformation of a targeted cell. The plasmid consist of a plasmid backbone. A "plasmid backbone" as used herein contains multiple genetic elements positional and sequentially oriented with other necessary genetic elements such that the nucleic acid in a nucleic acid cassette can be transcribed and when necessary translated in the transfected or

transduced cells. The term plasmid as used herein can refer to nucleic acid, e.g., DNA derived from a plasmid vector, cosmid, phagemid or bacteriophage, into which one or more fragments of nucleic acid may be inserted or cloned which encode for particular genes

A "viral vector" as used herein is one that is physically incorporated in a viral particle by the inclusion of a portion of a viral genome within the vector, e.g., a packaging signal, and is not merely DNA or a located gene taken from a portion of a viral nucleic acid. Thus, while a portion of a viral genome can be present in a plasmid of the present disclosure, that portion does not cause incorporation of the plasmid into a viral particle and thus is unable to produce an infective viral particle.

As used herein, the term "vector" refers to any genetic element, such as a plasmid, phage, transposon, cosmid, chromosome, virus, virion, etc., which is capable of replication when associated with the proper control elements and which can transfer gene sequences between cells. Thus, the term includes cloning and expression vehicles, as well as viral vectors.

As used herein, the term "integrating vector" refers to a vector whose integration or insertion into a nucleic acid (e.g., a chromosome) is accomplished via an integrase. Examples of "integrating vectors" include, but are not limited to, retroviral vectors, transposons, and adeno associated virus vectors.

As used herein, the term "integrated" refers to a vector that is stably inserted into the genome (i.e., into a chromosome) of a host cell.

As used herein, the term "genome" refers to the genetic material (e.g., chomosomes) of an organism.

As used herein, the term "exogenous gene" refers to a gene that is not naturally present in a host organism or cell, or is artificially introduced into a host organism or cell.

The term "gene" refers to a nucleic acid (e.g., DNA or RNA) sequence that comprises coding sequences necessary for the production of a polypeptide or precursor (e.g., proinsulin). The polypeptide can be encoded by a full length coding sequence or by any portion of the coding sequence so long as the desired activity or functional properties (e.g., enzymatic activity, ligand binding, signal transduction, etc.) of the full-length or fragment are retained. The term also encompasses the coding region of a structural gene and includes sequences located adjacent to the coding region on both the 5′ and 3′ ends for a distance of about 1 kb or more on either end such that the gene corresponds to the length of the full-length mRNA. The sequences that are located 5′ of the coding region and which are present on the mRNA are referred to as 5′ untranslated sequences. The sequences that are located 3′ or downstream of the coding region and which are present on the mRNA are referred to as 3′ untranslated

sequences. The term "gene" encompasses both cDNA and genomic forms of a gene. A genomic form or clone of a gene contains the coding region interrupted with non-coding sequences termed "introns" or "intervening regions" or "intervening sequences." Introns are segments of a gene which are transcribed into nuclear RNA (hnRNA); introns may contain regulatory elements such as enhancers. Introns are removed or "spliced out" from the nuclear or primary transcript; introns therefore are absent in the messenger RNA (mRNA) transcript. The mRNA functions during translation to specify the sequence or order of amino acids in a nascent polypeptide.

As used herein, the term "gene expression" refers to the process of converting genetic information encoded in a gene into RNA (e.g., mRNA, rRNA, tRNA, or snRNA) through "transcription" of the gene (i.e., via the enzymatic action of an RNA polymerase), and for protein encoding genes, into protein through "translation" of mRNA. Gene expression can be regulated at many stages in the process. "Up-regulation" or "activation" refers to regulation that increases the production of gene expression products (i.e., RNA or protein), while "down-regulation" or "repression" refers to regulation that decrease production. Molecules (e.g., transcription factors) that are involved in up-regulation or down-regulation are often called "activators" and "repressors," respectively.

Where "amino acid sequence" is recited herein to refer to an amino acid sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms, such as "polypeptide" or "protein" are not meant to limit the amino acid sequence to the complete, native amino acid sequence associated with the recited protein molecule.

As used herein, the terms "nucleic acid molecule encoding," "DNA sequence encoding," "DNA encoding," "RNA sequence encoding," and "RNA encoding" refer to the order or sequence of deoxyribonucleotides or ribonucleotides along a strand of deoxyribonucleic acid or ribonucleic acid. The order of these deoxyribonucleotides or ribonucleotides determines the order of amino acids along the polypeptide (protein) chain. The DNA or RNA sequence thus codes for the amino acid sequence.

As used herein, the term "variant," when used in reference to a protein, refers to proteins encoded by partially homologous nucleic acids so that the amino acid sequence of the proteins varies. As used herein, the term "variant" encompasses proteins encoded by homologous genes having both conservative and nonconservative amino acid substitutions that do not result in a change in protein function, as well as proteins encoded by homologous genes having amino acid substitutions that cause decreased (e.g., null mutations) protein function or increased protein function.

The terms "in operable combination," "in operable order," and "operably linked" as used herein refer to the linkage of nucleic acid sequences in such a manner that a nucleic acid molecule capable of directing the transcription of a given gene and/or the synthesis of a desired protein molecule is produced. The term also refers to the linkage of amino acid sequences in such a manner so that a functional protein is produced.

As used herein, the term "regulatory element" refers to a genetic element which controls some aspect of the expression of nucleic acid sequences. For example, a promoter is a regulatory element that facilitates the initiation of transcription of an operably linked coding region. Other regulatory elements are splicing signals, polyadenylation signals, termination signals, RNA export elements, internal ribosome entry sites, etc.

Transcriptional control signals in eukaryotes comprise "promoter" and "enhancer" elements. Promoters and enhancers consist of short arrays of DNA sequences that interact specifically with cellular proteins involved in transcription (Maniatis et al., Science 236:1237 [1987]). Promoter and enhancer elements have been isolated from a variety of eukaryotic sources including genes in yeast, insect and mammalian cells, and viruses (analogous control elements, i.e., promoters, are also found in prokaryotes). The selection of a particular promoter and enhancer depends on what cell type is to be used to express the protein of interest. Some eukaryotic promoters and enhancers have a broad host range while others are functional in a limited subset of cell types (for review see, Voss et al., Trends Biochem. Sci., 11:287 [1986]; and Maniatis et al., supra). For example, the SV40 early gene enhancer is very active in a wide variety of cell types from many mammalian species and has been widely used for the expression of proteins in mammalian cells (Dijkema et al, EMBO J. 4:761 [1985]). Two other examples of promoter/enhancer elements active in a broad range of mammalian cell types are those from the human elongation factor 1α gene (Uetsuki et al., J. Biol. Chem., 264:5791 [1989]; Kim et al., Gene 91:217 [1990]; and Mizushima and Nagata, Nuc. Acids. Res., 18:5322 [1990]) and the long terminal repeats of the Rous sarcoma virus (Gorman et al., Proc. Natl. Acad. Sci. USA 79:6777 [1982]) and the human cytomegalovirus (Boshart et al., Cell 41:521 [1985]).

As used herein, the term "promoter/enhancer" denotes a segment of DNA which contains sequences capable of providing both promoter and enhancer functions (i.e., the functions provided by a promoter element and an enhancer element, see above for a discussion of these functions). For example, the long terminal repeats of retroviruses contain both promoter and enhancer functions. The enhancer/promoter may be "endogenous" or "exogenous" or "heterologous." An "endogenous" enhancer/promoter is one which is naturally

linked with a given gene in the genome. An "exogenous" or "heterologous" enhancer/promoter is one which is placed in juxtaposition to a gene by means of genetic manipulation (i.e., molecular biological techniques such as cloning and recombination) such that transcription of that gene is directed by the linked enhancer/promoter.

The term "promoter," "promoter element," or "promoter sequence" as used herein, refers to a DNA sequence which when ligated to a nucleotide sequence of interest is capable of controlling the transcription of the nucleotide sequence of interest into mRNA. A promoter is typically, though not necessarily, located 5' (i.e., upstream) of a nucleotide sequence of interest whose transcription into mRNA it controls, and provides a site for specific binding by RNA polymerase and other transcription factors for initiation of transcription.

Promoters may be constitutive or regulatable. The term "constitutive" when made in reference to a promoter means that the promoter is capable of directing transcription of an operably linked nucleic acid sequence in the absence of a stimulus (e.g., heat shock, chemicals, etc.). In contrast, a "regulatable" promoter is one which is capable of directing a level of transcription of an operably linked nucleic acid sequence in the presence of a stimulus (e.g., heat shock, chemicals, etc.) which is different from the level of transcription of the operably linked nucleic acid sequence in the absence of the stimulus. Certain promoters are also known in the art to impart tissue-specificity and/or temporal/developmental specificity to expression of a nucleic acid sequence under control of such a promoter.

Eukaryotic expression vectors may also contain "viral replicons" or "viral origins of replication." Viral replicons are viral DNA sequences that allow for the extrachromosomal replication of a vector in a host cell expressing the appropriate replication factors. Vectors that contain either the SV40 or polyoma virus origin of replication replicate to high "copy number" (up to 104 copies/cell) in cells that express the appropriate viral T antigen. Vectors that contain the replicons from bovine papillomavirus or Epstein-Barr virus replicate extrachromosomally at "low copy number" (~100 copies/cell). However, it is not intended that expression vectors be limited to any particular viral origin of replication.

As used herein, the term "retrovirus" refers to a retroviral particle which is capable of entering a cell (i.e., the particle contains a membrane-associated protein such as an envelope protein or a viral G glycoprotein which can bind to the host cell surface and facilitate entry of the viral particle into the cytoplasm of the host cell) and integrating the retroviral genome (as a double-stranded provirus) into the genome of the host cell. The term "retrovirus" encompasses Oncovirinae (e.g., Moloney murine leukemia virus (MoMLV, also recited as simply "MLV" herein), Moloney murine sarcoma virus (MoMSV), and Mouse mammary

tumor virus (MMTV), Spumavirinae, amd Lentivirinae (e.g., Human immunodeficiency virus, Simian immunodeficiency virus, Equine infection anemia virus, and Caprine arthritis-encephalitis virus; See, e.g., U.S. Pat. Nos. 5,994,136 and 6,013,516, both of which are incorporated herein by reference).

As used herein, the term "retroviral vector" refers to a retrovirus that has been modified to express a gene of interest. Retroviral vectors can be used to transfer genes efficiently into host cells by exploiting the viral infectious process. Foreign or heterologous genes cloned (i.e., inserted using molecular biological techniques) into the retroviral genome can be delivered efficiently to host cells which are susceptible to infection by the retrovirus.

The term "Rhabdoviridae" refers to a family of enveloped RNA viruses that infect animals, including humans, and plants. The Rhabdoviridae family encompasses the genus Vesiculovirus which includes vesicular stomatitis virus (VSV), Cocal virus, Piry virus, Chandipura virus, and Spring viremia of carp virus (sequences encoding the Spring viremia of carp virus are available under GenBank accession number U18101). The G proteins of viruses in the Vesiculovirus genera are virally-encoded integral membrane proteins that form externally projecting homotrimeric spike glycoproteins complexes that are required for receptor binding and membrane fusion. The G proteins of viruses in the Vesiculovirus genera have a covalently bound palmititic acid (C16) moiety. The amino acid sequences of the G proteins from the Vesiculoviruses are fairly well conserved. For example, the Piry virus G protein share about 38% identity and about 55% similarity with the VSV G proteins (several strains of VSV are known, e.g., Indiana, New Jersey, Orsay, San Juan, etc., and their G proteins are highly homologous). The Chandipura virus G protein and the VSV G proteins share about 37% identity and 52% similarity. Given the high degree of conservation (amino acid sequence) and the related functional characteristics (e.g., binding of the virus to the host cell and fusion of membranes, including syncytia formation) of the G proteins of the Vesiculoviruses, the G proteins from non-VSV Vesiculoviruses may be used in place of the VSV G protein for the pseudotyping of viral particles. The G proteins of the Lyssa viruses (another genera within the Rhabdoviridae family) also share a fair degree of conservation with the VSV G proteins and function in a similar manner (e.g., mediate fusion of membranes) and therefore may be used in place of the VSV G protein for the pseudotyping of viral particles. The Lyssa viruses include the Mokola virus and the Rabies viruses (several strains of Rabies virus are known and their G proteins have been cloned and sequenced). The Mokola virus G protein shares stretches of homology (particularly over the extracellular and transmembrane domains) with the VSV G proteins which show about 31% identity and 48% similarity with the VSV G proteins. Preferred

G proteins share at least 25% identity, preferably at least 30% identity and most preferably at least 35% identity with the VSV G proteins. The VSV G protein from which New Jersey strain (the sequence of this G protein is provided in GenBank accession numbers M27165 and M21557) is employed as the reference VSV G protein.

As used herein, the term "lentivirus vector" refers to retroviral vectors derived from the Lentiviridae family (e.g., human immunodeficiency virus, simian immunodeficiency virus, equine infectious anemia virus, and caprine arthritis-encephalitis virus) that are capable of integrating into non-dividing cells (See, e.g., U.S. Pat. Nos. 5,994,136 and 6,013,516, both of which are incorporated herein by reference).

As used herein, the term "adeno-associated virus (AAV) vector" refers to a vector derived from an adeno-associated virus serotype, including without limitation, AAV-1, AAV-2, AAV-3, AAV-4, AAV-5, AAVX7, etc. AAV vectors can have one or more of the AAV wild-type genes deleted in whole or part, preferably the rep and/or cap genes, but retain functional flanking ITR sequences.

As used herein the term, the term "*in vitro*" refers to an artificial environment and to processes or reactions that occur within an artificial environment. In vitro environments can consist of, but are not limited to, test tubes and cell cultures. The term "in vivo" refers to the natural environment (e.g., an animal or a cell) and to processes or reaction that occur within a natural environment.

As used herein, the term "clonally derived" refers to a cell line that it derived from a single cell.

As used herein, the term "non-clonally derived" refers to a cell line that is derived from more than one cell.

As used herein, the term "passage" refers to the process of diluting a culture of cells that has grown to a particular density or confluency (e.g., 70% or 80% confluent), and then allowing the diluted cells to regrow to the particular density or confluency desired (e.g., by replating the cells or establishing a new roller bottle culture with the cells.

As used herein, the term "stable," when used in reference to genome, refers to the stable maintenance of the information content of the genome from one generation to the next, or, in the particular case of a cell line, from one passage to the next. Accordingly, a genome is considered to be stable if no gross changes occur in the genome (e.g., a gene is deleted or a chromosomal translocation occurs). The term "stable" does not exclude subtle changes that may occur to the genome such as point mutations.

As used herein, the term "cell culture" refers to any *in vitro* culture of cells. Included within this term are continuous cell lines (e.g., with an immortal phenotype), primary cell cultures, finite cell lines (e.g., non-transformed cells), and any other cell population maintained in vitro, including oocytes and embryos.

As used herein, the term "host cell" refers to any eukaryotic cell (e.g., mammalian cells, avian cells, amphibian cells, plant cells, fish cells, and insect cells), whether located *in vitro* or *in vivo*.

As used herein, the term "next-generation sequencing" or "NGS" can refer to sequencing technologies that have the capacity to sequence polynucleotides at speeds that were unprecedented using conventional sequencing methods (e.g., standard Sanger or Maxam-Gilbert sequencing methods). These unprecedented speeds are achieved by performing and reading out thousands to millions of sequencing reactions in parallel. NGS sequencing platforms include, but are not limited to, the following: Massively Parallel Signature Sequencing (Lynx Therapeutics); 454 pyro-sequencing (454 Life Sciences/Roche Diagnostics); solid-phase, reversible dye-terminator sequencing (Solexa/Illumina); SOLiD technology (Applied Biosystems); Ion semiconductor sequencing (ion Torrent); and DNA nanoball sequencing (Complete Genomics). Descriptions of certain NGS platforms can be found in the following: Shendure, er al., "Next-generation DNA sequencing," Nature, 2008, vol. 26, No. 10, 135-1 145; Mardis, "The impact of next-generation sequencing technology on genetics," Trends in Genetics, 2007, vol. 24, No. 3, pp. 133-141 ; Su, et al., "Next-generation sequencing and its applications in molecular diagnostics" Expert Rev Mol Diagn, 2011 , 11 (3):333-43; and Zhang et al., "The impact of next-generation sequencing on genomics", J Genet Genomics, 201, 38(3): 95-109.

The term "administration" refers to introducing a substance into a subject. In general, any route of administration may be utilized including, for example, parenteral (e.g., intravenous), oral, topical, subcutaneous, peritoneal, intraarterial, inhalation, vaginal, rectal, nasal, introduction into the cerebrospinal fluid, or instillation into body compartments. In some embodiments, administration is oral. Additionally or alternatively, in some embodiments, administration is parenteral. In some embodiments, administration is intravenous.

By "agent" is meant any small compound (e.g., small molecule), antibody, nucleic acid molecule, or polypeptide, or fragments thereof or cellular therapeutics such as allogeneic transplantation and/or CART-cell therapy.

The term "cancer" refers to a malignant neoplasm (Stedman's Medical Dictionary, 25th ed.; Hensyl ed.; Williams & Wilkins: Philadelphia, 1990). Exemplary cancers include, but are

not limited to, melanoma and ovarian cancer (e.g., cystadenocarcinoma, ovarian embryonal carcinoma, ovarian adenocarcinoma), with ovarian cancer specifically including clear cell ovarian cancer. Additional exemplary cancers include, but are not limited to, colorectal cancer (e.g., colon cancer, rectal cancer, colorectal adenocarcinoma), endometrial cancer (e.g., uterine cancer, uterine sarcoma), esophageal cancer (e.g., adenocarcinoma of the esophagus, Barrett's adenocarcinoma), and gastric cancer (e.g., stomach adenocarcinoma (STAD)), including, e.g., colon adenocarcinoma (COAD), oesophageal carcinoma (ESCA), rectal adenocarcinoma (READ) and uterine corpus endometrial carcinoma (UCEC). Other exemplary forms of cancer include, but are not limited to, diffuse large B-cell lymphoma (DLBCL), as well as the broader class of lymphoma such as Hodgkin lymphoma (HL) (e.g., B-cell HL, T-cell HL) and non-Hodgkin lymphoma (NHL) (e.g., B-cell NHL such as diffuse large cell lymphoma (DLCL) (e.g., diffuse large B-cell lymphoma (DLBCL)), follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), mantle cell lymphoma (MCL), marginal zone B-cell lymphomas (e.g., mucosa-associated lymphoid tissue (MALT) lymphomas, nodal marginal zone B-cell lymphoma, splenic marginal zone B-cell lymphoma), primary mediastinal B-cell lymphoma, Burkitt lymphoma, lymphoplasmacytic lymphoma (i.e., Waldenström's macroglobulinemia), hairy cell leukemia (HCL), immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma and primary central nervous system (CNS) lymphoma; and T-cell NHL such as precursor T-lymphoblastic lymphoma/leukemia, peripheral T-cell lymphoma (PTCL) (e.g., cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sezary syndrome), angioimmunoblastic T-cell lymphoma, extranodal natural killer T-cell lymphoma, enteropathy type T-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, and anaplastic large cell lymphoma); a mixture of one or more leukemia/lymphoma as described above;, hematopoietic cancers (e.g., myeloid malignancies (e.g., acute myeloid leukemia (AML) (e.g., B-cell AML, T-cell AML), myelodysplastic syndrome, myeloproliferative neoplasm, chronic myelomonocytic leukemia (CMML) and chronic myelogenous leukemia (CML) (e.g., B-cell CML, T-cell CML)) and lymphocytic leukemia such as acute lymphocytic leukemia (ALL) (e.g., B-cell ALL, T-cell ALL) and chronic lymphocytic leukemia (CLL) (e.g., B-cell CLL, T-cell CLL)); brain cancer (e.g., meningioma, glioblastomas, glioma (e.g., astrocytoma, oligodendroglioma), medulloblastoma); lung cancer (e.g., bronchogenic carcinoma, small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC), adenocarcinoma of the lung); acoustic neuroma; adenocarcinoma; adrenal gland cancer; anal cancer; angiosarcoma (e.g., lymphangiosarcoma, lymphangioendotheliosarcoma, hemangiosarcoma); appendix cancer; benign monoclonal gammopathy; biliary cancer (e.g.,

cholangiocarcinoma); bladder cancer; breast cancer (e.g., adenocarcinoma of the breast, papillary carcinoma of the breast, mammary cancer, medullary carcinoma of the breast); bronchus cancer; carcinoid tumor; cervical cancer (e.g., cervical adenocarcinoma); choriocarcinoma; chordoma; craniopharyngioma; connective tissue cancer; epithelial carcinoma; ependymoma; endotheliosarcoma (e.g., Kaposi's sarcoma, multiple idiopathic hemorrhagic sarcoma); Ewing's sarcoma; ocular cancer (e.g., intraocular melanoma, retinoblastoma); familiar hypereosinophilia; gall bladder cancer; gastrointestinal stromal tumor (GIST); germ cell cancer; head and neck cancer (e.g., head and neck squamous cell carcinoma, oral cancer (e.g., oral squamous cell carcinoma), throat cancer (e.g., laryngeal cancer, pharyngeal cancer, nasopharyngeal cancer, oropharyngeal cancer)); and multiple myeloma (MM)), heavy chain disease (e.g., alpha chain disease, gamma chain disease, mu chain disease); hemangioblastoma; hypopharynx cancer; inflammatory myofibroblastic tumors; immunocytic amyloidosis; kidney cancer (e.g., nephroblastoma a.k.a. Wilms' tumor, renal cell carcinoma); liver cancer (e.g., hepatocellular cancer (HCC), malignant hepatoma); leiomyosarcoma (LMS); mastocytosis (e.g., systemic mastocytosis); muscle cancer; myelodysplastic syndrome (MDS); mesothelioma; myeloproliferative disorder (MPD) (e.g., polycythemia vera (PV), essential thrombocytosis (ET), agnogenic myeloid metaplasia (AMM) a.k.a. myelofibrosis (MF), chronic idiopathic myelofibrosis, chronic myelocytic leukemia (CML), chronic neutrophilic leukemia (CNL), hypereosinophilic syndrome (HES)); neuroblastoma; neurofibroma (e.g., neurofibromatosis (NF) type 1 or type 2, schwannomatosis); neuroendocrine cancer (e.g., gastroenteropancreatic neuroendocrine tumor (GEP-NET), carcinoid tumor); osteosarcoma (e.g., bone cancer); papillary adenocarcinoma; pancreatic cancer (e.g., pancreatic andenocarcinoma, intraductal papillary mucinous neoplasm (IPMN), Islet cell tumors); penile cancer (e.g., Paget's disease of the penis and scrotum); pinealoma; primitive neuroectodermal tumor (PNT); plasma cell neoplasia; paraneoplastic syndromes; intraepithelial neoplasms; prostate cancer (e.g., prostate adenocarcinoma); rectal cancer; rhabdomyosarcoma; salivary gland cancer; skin cancer (e.g., squamous cell carcinoma (SCC), keratoacanthoma (KA), melanoma, basal cell carcinoma (BCC)); small bowel cancer (e.g., appendix cancer); soft tissue sarcoma (e.g., malignant fibrous histiocytoma (MFH), liposarcoma, malignant peripheral nerve sheath tumor (MPNST), chondrosarcoma, fibrosarcoma, myxosarcoma); sebaceous gland carcinoma; small intestine cancer; sweat gland carcinoma; synovioma; testicular cancer (e.g., seminoma, testicular embryonal carcinoma); thyroid cancer (e.g., papillary carcinoma of the thyroid, papillary thyroid carcinoma (PTC), medullary thyroid cancer); urethral cancer; vaginal cancer; and vulvar cancer (e.g., Paget's disease of the vulva).

Unless specifically stated or obvious from context, as used herein, the term "about" is understood as within a range of normal tolerance in the art, for example within 2 standard deviations of the mean. "About" can be understood as within 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1%, 0.05%, or 0.01% of the stated value.

In certain embodiments, the term "approximately" or "about" refers to a range of values that fall within 25%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or less in either direction (greater than or less than) of the stated reference value unless otherwise stated or otherwise evident from the context (except where such number would exceed 100% of a possible value).

Unless otherwise clear from context, all numerical values provided herein are modified by the term "about."

By "control" or "reference" is meant a standard of comparison. Methods to select and test control samples are within the ability of those in the art. Determination of statistical significance is within the ability of those skilled in the art, e.g., the number of standard deviations from the mean that constitute a positive result.

As used herein, the term "each," when used in reference to a collection of items, is intended to identify an individual item in the collection but does not necessarily refer to every item in the collection. Exceptions can occur if explicit disclosure or context clearly dictates otherwise.

As used herein, the term "subject" includes humans and mammals (e.g., mice, rats, pigs, cats, dogs, and horses). In many embodiments, subjects are mammals, particularly primates, especially humans. In some embodiments, subjects are livestock such as cattle, sheep, goats, cows, swine, and the like; poultry such as chickens, ducks, geese, turkeys, and the like; and domesticated animals particularly pets such as dogs and cats. In some embodiments (e.g., particularly in research contexts) subject mammals will be, for example, rodents (e.g., mice, rats, hamsters), rabbits, primates, or swine such as inbred pigs and the like.

Unless specifically stated or obvious from context, as used herein, the term "or" is understood to be inclusive. Unless specifically stated or obvious from context, as used herein, the terms "a", "an", and "the" are understood to be singular or plural.

Ranges can be expressed herein as from "about" one particular value, and/or to "about" another particular value. When such a range is expressed, another aspect includes from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent "about," it is understood that the particular value

forms another aspect. It is further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint. It is also understood that there are a number of values disclosed herein, and that each value is also herein disclosed as "about" that particular value in addition to the value itself. It is also understood that throughout the application, data are provided in a number of different formats and that this data represent endpoints and starting points and ranges for any combination of the data points. For example, if a particular data point "10" and a particular data point "15" are disclosed, it is understood that greater than, greater than or equal to, less than, less than or equal to, and equal to 10 and 15 are considered disclosed as well as between 10 and 15. It is also understood that each unit between two particular units are also disclosed. For example, if 10 and 15 are disclosed, then 11, 12, 13, and 14 are also disclosed.

Ranges provided herein are understood to be shorthand for all of the values within the range. For example, a range of 1 to 50 is understood to include any number, combination of numbers, or sub-range from the group consisting 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 as well as all intervening decimal values between the aforementioned integers such as, for example, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, and 1.9. With respect to sub-ranges, "nested sub-ranges" that extend from either end point of the range are specifically contemplated. For example, a nested sub-range of an exemplary range of 1 to 50 may comprise 1 to 10, 1 to 20, 1 to 30, and 1 to 40 in one direction, or 50 to 40, 50 to 30, 50 to 20, and 50 to 10 in the other direction.

The transitional term "comprising," which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. By contrast, the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.

The embodiments set forth below and recited in the claims can be understood in view of the above definitions.

Other features and advantages of the disclosure will be apparent from the following description of the preferred embodiments thereof, and from the claims. Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although

methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All published foreign patents and patent applications cited herein are incorporated herein by reference. All other published references, documents, manuscripts and scientific literature cited herein are incorporated herein by reference. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

The following detailed description, given by way of example, but not intended to limit the invention solely to the specific embodiments described, may best be understood in conjunction with the accompanying drawings.

FIGs. 1A to 1F display four schematic diagrams, a picture, and a graph, respectively, depicting an overview of self-reporting technology according to exemplary embodiments of the disclosure. FIG. 1A is a diagram showing that Virus-like Particles (VLPs) generated by endogenous or ectopic expression of gag or gag-like proteins allow for export of cellular contents from living cells. FIG. 1B is a diagram that is expanded from the inset square in FIG. 1A, which shows that proteins, lipids, metabolites, small molecules, RNA and/or DNA can be exported *via* VLPs. FIG. 1C is a diagram showing that VLPs are comprised of viral capsid proteins, with a core carrying analytes of interest. FIG. 1D is a diagram showing that VLPs can be collected from the same culture over time, and purified with immunoprecipitation (IP) – optionally via IP of cell line-specific and/or virion-specific tags – centrifugation, concentration *via* molecular weight cutoff filters, gradients, crowding agents (such as PEG), or a combination of the mentioned methods. FIG. 1E is a picture showing that if RNA is the analyte of interest, RNAseq libraries can be generated and sequenced (e.g., with Next Generation Sequencing (NGS) technology. FIG. 1F is a graph showing that time series measurements can be analyzed from the same biological samples, to provide longitudinal information about the same biological sample throughout time.

FIGs. 2A to 2D display a Western Blot, a dot plot, a schematic, and a dot plot, respectively, showing that flag-mediated immunoprecipitation of VLPs enabled clean RNAseq library construction with minimal background according to exemplary embodiments of the disclosure. FIG. 2A shows a Western Blot that was performed to measure production of Gag protein in lysate, VLP generation (measured by Gag protein in supernatant), and envelope-

based immunoprecipitation (measured by Gag protein detected after a flag immunoprecipitation). In this experiment; 293T cells were transfected with MLV gag, VSV-g (envelope), flag-VSV-g (flag-envelope) and/or pUC19 (negative control). FIG. 2B shows dot plot data of supernatants obtained from conditions where MLV gag was transfected, which demonstrated that the instant approach generated high quality RNAseq libraries, as measured by genes detected. FIG. 2C is a schematic showing a VLP with envelope glycoproteins, such as VSV-g (adapted electron cryo tomograph from Riedel *et al., J Struct Biol.* 2017). FIG. 2D shows dot plot data in which VLPs labeled with flag-VSV-g were demonstrated to have generated high quality RNAseq libraries after flag immunoprecipitation, as measured by genes detected. Background from VLPs without flag-labeled envelopes was identified to be negligible.

FIG. 3 provides a schematic diagram (top) and a graph (bottom) showing that affinity-tagged VLPs generated high quality RNAseq libraries that exhibited low background. Affinity-tag based immunoprecipitation (IP) was conducted to determine whether RNA could be captured and selectively purified from pseudotyped (flag-VSV-g+, or HA-VSV-g+) virus-like particles (VLPs). Utilizing two different cell types (293T and HT1080) and two different affinity tagged envelopes (flag-VSV-g, HA-VSV-g), high quality RNAseq libraries (quantified by genes detected) were generated when each supernatant was put through the matching immunoprecipitation. Conversely, poor quality RNAseq libraries (quantified by genes detected) were generated when each supernatant was put through an incorrect immunoprecipitation. These data were collected from cell-lines with stable, single-copy expression of gag and an affinity-labeled VSV-g, integrated via lentivirus.

FIG. 4 provides a schematic diagram (top) and a graph (bottom) showing that affinity-tagged envelopes can be used to non-destructively classify two distinct, exporting (gag+) cell-types from living co-culture. 293T and HT1080 VLP-producing cell lines (gag+) were co-cultured and supernatants were collected and processed via IP. Supernatants processed via flag-IP generated RNAseq libraries that classified as 293T cells, demonstrating that the flag-IP captured VLPs were indeed from 293Ts. Similarly, supernatants processed via HA-IP generated RNAseq libraries that classified as HT1080 cells, demonstrating that the HA-IP captured VLPs were indeed from HT1080s. These data were collected from cell-lines with stable, single-copy expression of gag and an affinity-labelled VSV-g, integrated via lentivirus.

FIG. 5 is a series of graphs showing that envelope-based multiplexing for live-cell monitoring is quantitative. RNAseq data show that quantitative transcriptional information can

be measured from live-cell co-cultures via purification of affinity-tagged VLPs *via* immunoprecipitation.

DETAILED DESCRIPTION OF THE INVENTION

The current disclosure relates, at least in part, to the identification of compositions and methods capable of inducing living cells to produce virus-like particles (VLPs) and allowing for highly specific isolation of such VLPs, which thereby enables real-time and/or time course assessment of VLP-captured analytes obtained from targeted living cells. Certain aspects of the instant disclosure feature introduction of a nucleic acid(s) encoding for (i) a VLP producing protein and (ii) an epitope-tagged viral surface protein into a living cell, which induces the living cell to produce VLPs that can then be readily isolated (e.g., by immunoprecipitation) *via* binding of the epitope tag. Such VLPs capture analytes from the living cells at the time of budding, meaning that assessment of VLP-encapsulated analytes (e.g., RNA) can provide a profile of such analytes in living cells over a time course, without harming the living cells (beyond any harm that might be done to the cells during transfection/transduction of the cells with the nucleic acid(s) encoding for the VLP producing protein and the epitope-tagged viral surface protein). When RNA is assessed as the VLP analyte, transcriptome profiling of the living cells can be performed in real time and/or over a time course while leaving the cells intact, which provides a significant benefit over other art-recognized transcriptome profiling methods, in contexts where survival of the cells for which transcriptome profiling is performed is advantageous.

In related aspects, distinct epitope tags can be employed to distinguish between different cell populations during analyte profiling (e.g., expression profiling) of living cells, even when such cell populations are mixed, which provides certain advantages over other art-recognized methods of analyte profiling.

Various expressly contemplated components of certain compositions and methods of the instant disclosure are considered in additional detail below.

Virus Like Particles (VLPs)

In certain aspects, the present disclosure provides compositions and methods that related to isolating and analyzing virus-like particles (VLPs) that present affinity-tagged envelope proteins. Virus-like particles (VLPs) are artificial protein structures that exhibit overall structure similar to their corresponding native viruses. VLPs resemble viruses in their self-assembly property but lack original infectious ability due to the genome modifications.

VLPs can be symmetrically built from hundreds to thousands of coat proteins, which can be genetically engineered to present a regular arrangement of epitopes on the desired positions of the outer surface. Compared with monomeric or oligomeric protein carriers, VLPs are able to provide not only a higher density of foreign proteins per particle but also support a distinctive three-dimensional conformation, which, without wishing to be bound by theory, has been described as especially important for the presentation of conformational epitopes. To date, VLPs have been recognized as one of the most promising and extensively studied molecular carriers or nanoparticles, for a variety of applications. (Zeltins *et al. Molecular biotechnology*, 53: 92-107).

Viral Gag Proteins

Certain aspects of the present disclosure relate to compositions and methods for isolating and analyzing VLPs generated *via* endogenous or ectopic expression of Gag (Group-specific antigen) or Gag-like proteins, which allow for export of cellular contents from living cells. The Gag polyprotein is a protein constructed from the nucleotide sequence of a retrovirus's RNA sequence. Gag polyproteins are used in the viral replication cycle of a retrovirus. The assembly and release of retrovirus particles from the cell membrane is directed by the Gag polyprotein. Utilizing methods of protein sequencing, scientists have begun to understand how these proteins can interact with the host cells and prevent infection. To date, no approach has been exploited in determining antiviral therapy utilizing Gag proteins due to the lack of knowledge concerning the structures and interactions responsible for assembly. The sequence of the Gag protein depends upon Gag-nucleic acid interactions. Nucleic acid sequences as short as 20-40 nucleotides can support VLP assembly *in vitro*. Since the Gag protein is the fundamental building block of the retrovirus particles, one expression of the gene into the Gag protein is sufficient to prompt replication of VLPs. The Gag protein itself has multiple domains within the complex. This multi-domain of the Gag protein participates in interactions with lipids in the plasma membrane, RNAs, and other Gag molecules. Gag proteins undergo conformational changes during virus particle assembly. In a Gag protein there is an N-terminal matrix domain (MA) and a C-terminal nucleocapsid domain (NC). Although both domains are positively charged and have affinities for negatively charged ions, the matrix domain has a high affinity for lipids due to the presence of phosphatidyl inositol bisphosphate, while the nucleocapsid domain has a high affinity for nucleic acids. Without wishing to be bound by theory, it is believed that this affinity allows for the Gag protein to become rod-like

upon entering the plasma membrane of the nucleous that contains nucleic acids. (Rein *et al. Trends Biochem Sci.* 36(7):373-80).

Exemplary Gag and Gag-like proteins include, but are not limited to, a retrovirus gag protein (e.g., a HIV Gag viral protein (e.g., HIV-1 NL43 Gag (GenBank serial number AAA44987), a simian immunodeficiency virus (SIV) Gag viral protein (e.g., SIVmac239 Gag (GenBank serial number CAA68379)), or a murine leukemia virus (MLV) Gag viral protein, such as GenBank serial number S70394).

MLV Gag viral protein (SEQ ID NO: 1)

MGQAVTTPLSLTLDHWKDVERTAHNLSVEVRKRRWVTFCSAEWPTFNVGWPRDGT
FNPDIITQVKIKVFSPGPHGHPDQVPYIVTWEAIAVDPPPWVRPFVHPKPPLSLPPSAPS
LPPEPPLSTPPQSSLYPALTSPLNTKPRPQVLPDSGGPLIDLLTEDPPPYRDPGPPSPDG
NGDSGEVAPTEGAPDPSPMVSRLRGRKEPPVADSTTSQAFPLRLGGNGQYQYWPFSS
SDLYNWKNNNPSFSEDPAKLTALIESVLLTHQPTWDDCQQLLGTLLTGEEKQRVLLE
ARKAVRGEDGRPTQLPNDINDAFPLERPDWDYNTQRGRNHLVHYRQLLLAGLQNA
GRSPTNLAKVKGITQGPNESPSAFLERLKEAYRRYTPYDPEDPGQETNVAMSFIWQS
APDIGRKLERLEDLKSKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEERRRAEDV
QREKERDRRRHREMSKLLATVVSGQRQDRQGGERRRPQLDHDQCAYCKEKGHWA
RDCPKKPRGPRGPRPQASLLTLDD

Additional exemplary Gag and Gag-like proteins include, but are not limited to, a retrovirus matrix protein, a rhabdovirus matrix protein M protein (e.g., a vesicular stomatis virus (VSV) M protein (GenBank serial number NP041714)), a filovirus viral core protein (e.g., an Ebola VP40 viral protein (e.g., Ebola virus VP40 (GenBank serial number AAN37506))), a Rift Valley Fever virus N protein (e.g., RVFV N Protein (GenBank serial number NP049344)), a coronavirus M, E and NP protein (e.g., GenBank serial number NP040838 for NP protein, NP 040835 for M protein, CAC39303 for E protein of Avian Infections Bronchitis Virus and NP828854 for E protein of the SARS virus)), a bunyavirus N protein (GenBank serial number AAA47114)), an influenza M1 protein, a paramyxovirus M protein, an arenavirus Z protein (e.g., a Lassa Fever Virus Z protein), and combinations thereof. Appropriate surface glycoproteins and/or viral RNA may be included to form the VLP.

In some embodiments, nonenveloped virus capsid proteins can be used. Examples of non-enveloped viruses include those of the virus families *Adenoviridae*, *Papovaviridae*, *Parvoviridae*, and *Anelloviridae*.

Without wishing to be bound by theory, Gag proteins are believed to be the core structural proteins of a retrovirus.

Retroviruses

Retroviruses refer to a family of viruses which have RNA and reverse transcriptase (RNA-dependent DNA polymerase), of which the latter is essential to the first stage of its self-replication for synthesizing complementary DNA on the base of template RNA of the virus. Retroviruses can be categorized into Orthoretrovirinae (includes oncoviruses and lentiviruses) and Spumaretrovirinae. The oncoviruses are thus termed because they can be associated with cancers and malignant infections. There may be mentioned, for example, leukemogenic viruses such as the avian leukemia virus (ALV), the murine leukemia virus (MULV), also called Moloney virus or simply MLV at some instances herein, the Abelson leukemia virus, the murine mammary tumor virus, the Mason-Pfizer monkey virus (or MPMV), the feline leukemia virus (FELV), human leukemia viruses such as HTLV1 (also,named HTLV-I) and HTLV2 (also named HTLV-II), the simian leukemia virus or STLV, the bovine leukemia virus or BLV, the primate type D oncoviruses, the type B oncoviruses which are inducers of mammary tumors, or oncoviruses which cause a rapid cancer (such as the Rous sarcoma virus or RSV).

Although the term "oncovirus" is still commonly used, other terms can also be used such as Alpharetrovirus for avian leukosis virus and Rous sarcoma virus; Betaretrovirus for mouse mammary tumor virus; Gammaretrovirus for murine leukemia virus and feline leukemia virus; Deltaretrovirus for bovine leukemia virus and human T-lymphotropic virus; and Epsilonretrovirus for Walleye dermal sarcoma virus. The lentiviruses, such as Human Immunodeficiency Virus (HIV, also known as HTLV-III or LAV for lymphotrophic adenovirus and which can be distinguished within HTV-1 and HTV-2), are thus named because they are responsible for slow-progressing pathological conditions which very frequently involve immunosuppressive phenomena, including AIDS. Among the lentiviruses, the visna/maedi virus (or MW/Visna), equine infectious anemia virus (EIAV), caprine arthritis encephalitis virus (CAEV), simian immunodeficiency virus (SIV) can also be cited (See, e.g., WO2015001518A1, which is incorporated herein by reference).

The spumaviruses manifest fairly low specificity for a given cell type or a given species, and they are sometimes associated with immunosuppressive phenomena; that is the case, for example, for the simian foamy virus (or SFV), also named chimpanzee simian virus, the human

foamy virus (or HFV), bovine syncytial virus (or BSV), feline syncytial virus (FSV) and the feline immunodeficiency virus.

Adeno-Associated Viruses (AAV)

Adeno-associated viruses (AAV) are small (about 20 nm) nonenveloped icosahedric ssDNA viruses, which depend on helper viruses (e.g., adenovirus or herpes simplex virus) for replication. To date, nine human serotypes have been characterized. About 80% of the population has detectable levels of anti-AAV antibodies, but there is no discernable pathology association with this virus. This fact and the ability of AAV to mediate transgene integration into a specific site in the human genome have made it an important candidate for use in gene therapy. The resulting knowledge about capsid structure and tolerance for peptide insertions has been described for use in the design of genome-free AAV-like particles (AAVLPs) as a novel high-density system for peptide vaccines. (Manzano-Szalai *et al. Viral Immunol.* 2014 Nov 1; 27(9): 438–448). It is expressly contemplated herein that AAV VLPs can be used in the compositions and methods of the instant disclosure.

Isolation and Purification of VLPs

In certain aspects, the compositions and methods of the present disclosure relate to isolating and analyzing virus-like particles (VLPs), optionally those presenting cell line specific affinity-tagged envelope proteins. VLPs of the instant disclosure can be isolated and purified by many methods including, but not limited to, immunoprecipitation (IP), gradient centrifugation, chromatography (e.g., gel filtration chromatography), assays, fractionation, quantitation, and electrophoresis. Certain aspects of the instant disclosure present immunoprecipitation that utilizes an affinity tagged viral envelope protein for VLP isolation and ultimate compilation of a clean RNA sequence library possessing minimal background. Immunoprecipitation (IP) is a method used to isolate a specific antigen from a mixture, using the antigen-antibody interaction. Antigens isolated by IP are typically analyzed by SDS-PAGE or Western blotting. In IP, an antibody is added first to a mixture containing an antigen, and incubated to allow antigen-antibody complexes to form. Subsequently, the antigen-antibody complexes are incubated with an immobilized antibody against the primary antibody (secondary antibody) or with protein A/G-coated beads to allow them to absorb the complexes. The beads are then thoroughly washed, and the antigen is eluted from the beads by an acidic solution or SDS. If suitable antibody is not available, the target molecule can be fused to a protein tag by recombinant DNA techniques, and IP can proceed using an antibody to the tag (pull-down assay).

In certain aspects, the present disclosure relates to compositions and methods for isolating and analyzing virus-like particles (VLPs) having cell line specific affinity-tagged envelopes (such as FLAG (epitope tag) tagged viral envelope (VSV-g)). Epitope tagging is a procedure whereby a short amino acid sequence recognized by a preexisting antibody is attached to a protein under study to allow its recognition by the antibody in a variety of *in vitro* or *in vivo* settings. A primary advantage of epitope tagging is that the time and expense associated with generating and characterizing antibodies against multiple proteins is obviated. However, epitope tagging offers a number of additional advantages such as: it allows tracking of closely related proteins without fear of spurious results resulting from cross-reactive antibodies; the intracellular location of epitope-tagged proteins can be identified in immunofluorescence experiments in a similarly well-controlled manner, without fear of cross-reactivity with the endogenous protein; the epitope-tagging approach can be particularly useful for discriminating among otherwise similar gene products that cannot be distinguished using conventional antibodies. For example, epitope tagging permits discrimination of individual members of closely related protein families or the identification of *in vitro*-mutagenized variants in the context of endogenous wild-type protein(s).

As specifically exemplified herein, a Vesicular Stomatitis Virus (VSV) glycoprotein was epitope tagged to improve targeted isolation of VLPs. An exemplary sequence for VSV glycoprotein is:

VSV-G Envelope Protein (VSV Glycoprotein; SEQ ID NO: 2) precursor:

MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTA
LQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESI
EQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGK
CSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYF
AYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTS
VDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYF
ETRYIRVDIAAPILSRMVGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPL
YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGW
FSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK

The initial 16 amino acids of the VSV-G envelope protein precursor are removed during processing, resulting in the mature form of the VSV-G Envelope Protein (VSV Glycoprotein, mature; SEQ ID NO: 21):

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADG
WMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQS
CGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHS
DYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSL
CQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRM
VGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSS
KAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLI
GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK

In some embodiments, a mutagenized VSV-G protein is employed. Optionally, mutagenesis of VSV-G protein produces a VSV-G protein that prevents VLP uptake. Examples of such VSV-G protein mutations include K47 and R354 VSV-G mutants (see Nikolic *et al. Nature Communications*, volume 9, Article number: 1029 (2018)).

VSV-G K47A Mutant Envelope Protein (VSV Glycoprotein, mature; SEQ ID NO: 22):
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADG
WMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQS
CGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHS
DYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSL
CQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRM
VGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSS
KAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLI
GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK

VSV-G R354A Mutant Envelope Protein (VSV Glycoprotein, mature; SEQ ID NO: 23):
KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADG
WMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQS
CGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHS
DYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSL
CQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRM
VGMISGTTTEAELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLS
SKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLI
GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK

VSV-G K47A, R354A Mutant Envelope Protein (VSV Glycoprotein, mature; SEQ ID NO: 28):

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADG
WMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQS
CGYATVTDAEAVIVQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHS
DYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSL
CQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRM
VGMISGTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLS
SKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFFFIIGLII
GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK

In certain aspects, targeted molecules used in the isolation of VLPs *via* IP or other such technique are viral surface envelope glycoproteins, which can include, but are not limited to, a retrovirus glycoprotein (e.g., a human immunodeficiency virus (HIV) envelope glycoprotein (e.g., HIVSF162 envelope glycoprotein (GenBank serial number M65024)), a simian immunodeficiency virus (SIV) envelope glycoprotein (e.g., SIVmac239 envelope glycoprotein (GenBank serial number M33262)), a simian-human immunodeficiency virus (SHIV) envelope glycoprotein (e.g., SHIV-89.6p envelope glycoprotein (GenBank serial number U89134)), a feline immunodeficiency virus (FIV) envelope glycoprotein (e.g., feline immunodeficiency virus envelope glycoprotein (GenBank serial number L00607)), a feline leukemia virus envelope glycoprotein (e.g., feline leukemia virus envelope glycoprotein (GenBank serial number M12500)), a bovine immunodeficiency virus envelope glycoprotein (e.g., bovine immunodeficiency virus envelope glycoprotein (GenBank serial number NC001413)), a bovine leukemia virus envelope glycoprotein (GenBank serial number AF399703), an equine infectious anemia virus envelope glycoprotein (e.g., equine infectious anemia virus envelope glycoprotein (GenBank serial number NC001450)), a human T-cell leukemia virus envelope glycoprotein (e.g., human T-cell leukemia virus envelope glycoprotein (GenBank serial number AF0033817)), and a mouse mammary tumor virus envelope glycoprotein (MMTV)), a bunyavirus glycoprotein (e.g., a Rift Valley Fever virus (RVFV) glycoprotein, (e.g., RVFV envelope glycoprotein (GenBank serial number M11157))), an arenavirus glycoprotein (e.g., a Lassa fever virus glycoprotein (GenBank serial number AF333969))), a filovirus glycoprotein (e.g., an Ebola virus glycoprotein (GenBank serial number NC002549)), a corona virus glycoprotein (GenBank serial number SARS coronavirus spike protein AAP13567), an influenza virus glycoprotein (GenBank serial number V01085)), a paramyxovirus glycoprotein

(GenBank serial number NC002728 for Nipah virus F and G proteins), a rhabdovirus glycoprotein (GenBank serial number NP049548)) (e.g., a Vesicular Stomatitis Virus (VSV) glycoprotein as exemplified), an alphavirus glycoprotein (GenBank serial number AAA48370 for Venezuelan equine encephalomyelitis (VEE)), a flavivirus glycoprotein (GenBank serial number NC001563 for West Nile virus) (e.g., a Hepatitis C Virus glycoprotein), a Herpes Virus glycoprotein (e.g., a cytomegalovirus glycoprotein), and combinations thereof.

In certain embodiments, nonenveloped capsid proteins can be used in the compositions and methods of the instant disclosure, such as capsid proteins from the virus families *Adenoviridae*, *Papovaviridae*, *Parvoviridae*, and *Anelloviridae*. In this context, the capsid can be mutagenized to prevent VLP uptake by neighboring cells, and an affinity tag can be optionally introduced to the capsid for purification. Also, the VLP can be purified with antibodies that bind to a non-tagged capsid.

In some embodiments, the VLPs naturally incorporate host membrane proteins, and VLPs can be purified by affinity-tagged host membrane proteins, or by using antibodies against host membrane proteins.

Exemplary epitope tags that can be attached to a targeted molecule can include, but are not limited to FLAG (DYKDDDDK; SEQ ID NO: 3), 6 x His (HHHHHH; SEQ ID NO: 4), HA (YPYDVPDYA; SEQ ID NO: 5), c-myc (EQKLISEEDL; SEQ ID NO: 6), V5 tag (GKPIPNPLLGLDST; SEQ ID NO: 7), AU1 tag (DTYRYI; SEQ ID NO: 8), AU5 tag (TDFYLK; SEQ ID NO: 9), Glu-Glu tag (EYMPME; SEQ ID NO: 10), OLLAS (SGFANELGPRLMGK; SEQ ID NO: 11), T7 tag (MASMTGGQQMG; SEQ ID NO: 12), VSV-G tag (YTDIEMNRLGK; SEQ ID NO: 13), E-Tag (GAPVPYPDPLEPR; SEQ ID NO: 14), S-Tag (KETAAAKFERQHMDS; SEQ ID NO: 15), HSV tag (SQPELAPEDPED; SEQ ID NO: 16), KT3 tag (KPPTPPPEPET; SEQ ID NO: 17), TK15 tag, GST tag, Protein A tag, CD tag, Strep-Tag (WSHPQFEK; SEQ ID NO: 18), MBP tag, CBD tag, Avi tag (CGLNDIFEAQKIEWHE; SEQ ID NO: 19), CBP tag, TAP tag, and SF-TAP tag. It is noted that in certain aspects, the above-referenced VSV-G tag is excluded from the above-recited list of contemplated epitope tags for inclusion in the compositions and methods of the instant disclosure.

As also noted above, in certain embodiments, purification of non-tagged envelope proteins (for enveloped VLPs) and/or non-tagged capsid proteins (for nonenveloped VLPs) can be performed using antibodies and/or affinity-binding methods.

Viral Transfection of Mammalian Cells

In certain aspects, the compositions and methods of the present disclosure relate to production of virus-like particles (VLPs) using viral vector-mediated transfection of nucleic acids that encode for VLP-inducing agents. Viral vectors have received much attention in recent years and have become powerful tools for gene delivery *in vitro* and *in vivo*. In cultured cells, viruses are primarily used to achieve stable genomic integration and an inducible expression of transgenes. *In vivo*, viruses are often the only viable option when aiming at efficiently introducing transgenes into specific cell types, as is needed, for instance, in gene therapy. Virus-mediated transfection, also known as transduction, offers a means to reach hard-to-transfect cell types for protein overexpression or knockdown, and it is the most commonly used method in clinical research. Adenoviral, oncoretroviral, and lentiviral vectors have been used extensively for gene delivery in mammalian cell culture and *in vivo*. Other well-known examples for viral gene transfer include baculovirus and vaccinia virus-based vectors. Any of these and other art-recognized viral gene transfer systems are contemplated for use in the context of the instant disclosure.

A typical transduction protocol involves engineering of the recombinant virus carrying the transgene, amplification of recombinant viral particles in a packaging cell line, purification and titration of amplified viral particles, and subsequent infection of the cells of interest. While the achieved transduction efficiencies in primary cells and cell lines are quite high (~90–100%), only cells carrying the viral-specific receptor can be infected by the virus. It is also important to note that the packaging cell line used for viral amplification needs to be transfected with a non-viral transfection method

Suitable mammalian cells that can be used for viral transduction include, but are not limited to, primary cells and cell lines, where suitable cell lines include, but are not limited to, 293 cells, COS cells, HeLa cells, Vero cells, 3T3 mouse fibroblasts, C3H10T1/2 fibroblasts, CHO cells, and the like. Non-limiting examples of suitable host cells include, e.g., HeLa cells (e.g., American Type Culture Collection (ATCC) No. CCL-2), CHO cells (e.g., ATCC Nos. CRL9618, CCL61, CRL9096), 293 cells (e.g., ATCC No. CRL-1573), Vero cells, NIH 3T3 cells (e.g., ATCC No. CRL-1658), Huh-7 cells, BHK cells (e.g., ATCC No. CCL10), PC12 cells (ATCC No. CRL1721), COS cells, COS-7 cells (ATCC No. CRL1651), RAT1 cells, mouse L cells (ATCC No. CCLI.3), human embryonic kidney (HEK) cells (ATCC No. CRL1573), HLHepG2 cells, and the like.

In certain embodiments, exemplary mammalian cells for viral transduction are primary rat cortical neurons and/or primary rat hippocampal neurons, optionally those obtained from microsurgically dissected tissue, *e.g.*, from E18 Sprague Dawley Rat.

Viral vectors have been employed in the study of various models of diseases such as metabolic, cardiovascular, muscular, hematologic, ophthalmologic, and infectious diseases and different types of cancer. Viral vectors such a retroviruses, adenoviruses, and herpes simplex viruses have been used in animal models and clinical trials of diseases such as, but not limited to, anaplastic thyroid cancer, carcinoma, hepatocellular carcinoma, glioma, hemophilia, Alzheimer's disease, sensory neuropathy, acquired immunodeficiency syndrome (AIDS), melanoma, Huntington's disease, and glioblastoma (Lundstrom. *Diseases*. 6(2) 42).

Neuronal Cell Disease Models

Animal modeling of human disease is a cornerstone to basic scientific studies of disease mechanisms and pre-clinical studies of potential therapies. Rapid progress in *in vitro*, *in vivo*, and *ex vivo* animal modeling has led to advancements in the understanding of fundamental disease mechanisms of many central nervous system (CNS) disorders, including but not limited to, initial cell death and later repair in stroke, motor and non-motor pathologies in Parkinson's disease, and axonal regeneration in peripheral and optic nerve injury, among many others. Ideally, animal modeling produces basic insights, new views of the human disease, and preclinical trials of novel therapies (Chesselet *et al. Neurotherapeutics*. 9(2): 241-244).

Many animal models have been used in the study of neurological disease such as rodents (rat and mice) and primates. The mouse model has been particularly studied extensively as a neurological disease model. The common house mouse (*Mus musculus*) has a genome with 97% homology to the human genome. Mouse models of neurological disorders can be usefully divided into whether or not the model is heritable. Human neurological disorders with a mutant gene component make ideal candidates for modelling via gene manipulation. It follows then that human neurological disorders with an identified underlying genetic component, for example Alzheimer's disease, have been extensively modelled using genetically manipulated mouse models. Alternatively an interesting neurological phenotype may be identified as a result of a spontaneous mutation in the wild type mouse population, for example the stargazer mouse. These spontaneous mutant mouse models are then bred to sustain the appropriate phenotype of interest. Clearly neurological disorders also have heritable traits that do not include mutant gene components but are well characterized risk factors for the disorder, for example the Apoe4 allele in AD. As these traits can be inherited from generation to generation they can also be included as heritable trait models. Mouse models that do not carry a heritable component are focused on replicating a phenotype characteristic of the relevant disorder. Those human disorders that do not have a defined genetic component, or in which a complex multi-gene

interacting system is under investigation, are more readily modelled using non heritable mouse models that have an identified robust phenotype and are acquired by physical manipulation (Harper. *BBA*. 10: 785-795).

Where animal models are employed, in some embodiments, specificity can be achieved through delivery, such as *via* use of a pseudotyped virus that only infects neurons, or a subset of neurons, and/or passes the blood brain barrier. For example, the AAV-PHP.B2 capsid can be used (from www.nature.com/articles/nbt.3440) to generate AAV carrying the VLP-inducing and envelope transgenes. This AAV can be administered *via* IV, allowing for delivery of the transgenes to the brain. Cerebral spinal fluid (CSF) can then be harvested from the animal to measure transcriptomes in different structures in the brain (such as the hippocampus), as well as different cell types in the brain (such as glial cells).

Neuronal Tissue-Specific Promoters

In certain aspects, the compositions and methods of the present disclosure include components that impart tissue-specificity to formation of particular types of VLPs. In one exemplified embodiment, to successfully label VLPs from excitatory neurons, a CamKII promoter can be used to drive expression of both a VLP producing protein, such as MLV Gag, as well as a labeled envelope protein, such as FLAG-VSVG. Meanwhile, to successfully label VLPs from inhibitory neurons, a mDlx promoter can be used to drive expression of both a VLP producing protein such as MLV Gag, as well as a labeled envelope protein, such as HA-VSVG. Such a system allows for direct comparison in real-time (and across a time course) of excitatory neuron transcriptomes vs. inhibitory neuron transcriptomes, from living cells of each respective type, even in mixed culture. Examples of neural tissue-specific promoters that can be employed in the compositions and methods of the instant disclosure include, but are not limited to, mDlx, CamKII, Syn1, NSE, PDGF and Ta1.

Compound Screening in Model Systems

Model systems, including laboratory animals, microorganisms, and cell- and tissue-based systems, are central to the discovery and development of new and better drugs for the treatment of human disease. Model systems such as animal models are essential for translation of drug findings from bench to bedside. Hence, critical evaluation of the face and predictive validity of these models is important. Reversely, clinical bedside findings that were not predicted by animal testing should be back translated and used to refine the animal models. Design, execution and reporting of results from animal model systems help to make preclinical

data more reproducible and translatable to the clinic. Design of an animal model strategy is part of the translational plan rather than (a) single experiment(s). Data from animal models are essential in predicting the clinical outcome for a specific drug in development. Review, standardization and refinement of animal models by disease expert groups helps to improve rigor of animal model testing. It is important that the applied animal models are validated fit-for-purpose according to stringent criteria and reproducible. During drug development fit-for-purpose animal models are key for success in clinical translation, financial investments and support from the government to develop, optimize, validate and run such translation tools are important. Over time, this will be of benefit for patients and healthcare institutions. Preclinical testing of a drug in an animal model is not a prerequisite for regulatory agencies before entering clinical trials, but does unquestionably provide valuable data on the expected clinical performance of the drug. Hence, testing in animal models is largely recommended from both a business and patient perspective. In addition, inclusion of safety parameters in animal models will help to build the required safety data package of drugs in development (Denayer *et al. Translational Medicine*. 2, 5-11).

It is herein expressly contemplated that the compositions and methods of the instant disclosure can be applied to a number of model systems, to enable assessment of real-time transcriptome monitoring of living cells in their native environment across a time course, optionally in response to administration of agents including, *e.g.*, lead drug compounds, screening compounds, etc. Such real-time/time course transcriptome information is contemplated to aid identification of drug impact upon oncogenesis, cell growth, toxicity and/or drug efficacy for any number of other uses, to the full extent that such real-time/time course transcriptome information can direct compound/lead agent selection, etc.

It is also expressly contemplated that, in certain embodiments, *e.g.*, where the differences between a pathological transcriptome and a normal transcriptome are known, combinations of drugs (including small molecules, biologics, modified nucleic acids, DNA-targeting CRISPR-Cas systems, RNA-targeting CRISPR-Cas systems, TALENs, zinc finger nucleases) can be measured from a living animal to pair phenotype (and/or behavior) with the resulting transcriptome.

Expression Vector Promoters

An expression vector, otherwise known as an expression construct, is commonly a plasmid or virus designed for gene expression in cells. The vector is used to introduce a specific

gene into a target cell, and can commandeer the cell's mechanism for protein synthesis to produce the protein encoded by the gene. Expression vectors are a basic tool in biotechnology for the production of proteins. The vector is engineered to contain regulatory sequences that act as enhancer and promoter regions and lead to efficient transcription of the gene carried on the expression vector. The promoters for cytomegalovirus (CMV) and SV40 are commonly used in mammalian expression vectors to drive gene expression. Non-viral promoters, such as the elongation factor (EF)-1 promoter, are also known.

CMV Promoter is commonly included in vectors used in genetic engineering work conducted in mammalian cells, as it is a strong promoter that drives constitutive expression of genes under its control. This promoter has been used to express a plethora of eukaryotic gene products and is used for specialty protein production, gene therapy, and DNA-based vaccination, among other applications.

The CMV promoter has the following sequence (SEQ ID NO: 20):

TAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTA
CATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATT
GACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGA
CGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGT
ATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTG
GCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTAC
GTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGC
GTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAA
TGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAAC
TCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATA
AGCAGAGCTGGTTTAGTGAACCGTCAG

The CAG promoter has the following sequence (SEQ ID NO: 27):

ACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCAT
AGCCCATATTGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTG
ACCGCCCAACGACCCCCGCCCCTTGACGTCAATAATGACGTATGTTCCCATAGTA
ACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTG
CCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGT
CAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGAC

TTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTGTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCA
AGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGG
ACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCG
TGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCC
TGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCC
AGCCTCCCCTCGAAGCTTTACATGTGGTACCGAGCTCGGATCCTGAGAACTTCAG
GGTGAGTCTATGGGACCCTTGATGTTTTCTTTCCCCTTCTTTTCTATGGTTAAGTTC
ATGTCATAGGAAGGGGAGAAGTAACAGGGTACACATATTGACCAAATCAGGGTA
ATTTTGCATTTGTAATTTTAAAAAATGCTTTCTTCTTTTAATATACTTTTTTGTTTA
TCTTATTTCTAATACTTTCCCTAATCTCTTTCTTTCAGGGCAATAATGATACAATG
TATCATGCCTCTTTGCACCATTCTAAAGAATAACAGTGATAATTTCTGGGTTAAG
GCAATAGCAATATTTCTGCATATAAATATTTCTGCATATAAATTGTAACTGATGT
AAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTATT
TTATGGTTGGGATAAGGCTGGATTATTCTGAGTCCAAGCTAGGCCCTTTTGCTAA
TCATGTTCATACCTCTTATCTTCCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGT
GTGCTGGCCCATCACTTTGGC

SV40 Promoter (Simian Virus 40 promoter) contains the SV40 enhancer promoter region and origin of replication (part no. GA-ori-00009.1) for high-level expression and replication in cell lines expressing the large T antigen (e.g. COS-7 and 293T cells). It does not replicate episomally in the absence of the SV40 large T antigen. The SV40 promoter is weak in B cells, but SV40 exhibits high activity in T24 and HCV29 human bladder urethelium carcinoma cell lines.

Human elongation factor-1 alpha (EF-1 alpha) or EF-1 is a constitutive non-viral promoter of human origin that can be used to drive ectopic gene expression in various *in vitro* and *in vivo* contexts. EF-1 alpha is often useful in conditions where other promoters (such as CMV) have diminished activity or have been silenced (as in embryonic stem cells).

Mammalian Cell Culture

In certain aspects, the instant disclosure describes methods and compositions designed to obtain VLP-encapsulated analyte data (e.g., real-time/time course transcriptome data) from living mammalian cells, optionally in cell culture. Mammalian cell culture is used widely in academic, medical and industrial settings. It has provided a means to study the physiology and

biochemistry of the cell, and developments in the fields of cell and molecular biology have required the use of reproducible model systems, which cultured cell lines are especially capable of providing. For medical use, cell culture provides test systems to assess the efficacy and toxicology of potential new drugs. Large-scale mammalian cell culture has allowed production of biologically active proteins, initially production of vaccines and then recombinant proteins and monoclonal antibodies; meanwhile, recent innovative uses of cell culture include tissue engineering, as a means of generating tissue substitutes.

Mammalian cells can be isolated from tissues for *ex vivo* culture in several ways. Cells can be easily purified from blood. However, only the white cells are capable of growth in culture. Cells can be isolated from solid tissues by digesting the extracellular matrix using enzymes such as collagenase, trypsin, or pronase, before agitating the tissue to release the cells into suspension. Alternatively, pieces of tissue can be placed in growth media, and the cells that grow out are available for culture. This method is known as explant culture. Cells that are cultured directly from a subject are known as primary cells. With the exception of some derived from tumors, most primary cell cultures have limited lifespan (Voight *et al. Journal of Molecular and Cellular Cardiology. 86: 187–98).* An established or immortalized cell line has acquired the ability to proliferate indefinitely either through random mutation or deliberate modification, such as artificial expression of the telomerase gene. Numerous cell lines are well established as representative of particular cell types. Examples of commonly used mammalian cell lines include HEK293T cells, VERO, BHK, HeLa, CV1 (including Cos), MDCK, 293, 3T3, myeloma cell lines (e.g., NSO, NS 1), PC12, W138 cells, and Chinese hamster ovary (CHO) cells, among many other examples (Langdon *et al. Molecular Biomethods Handbook.* 861-873).

Mammalian Cell Transfection Methods

Mammalian cell transfection is a technique commonly used to express exogenous DNA or RNA in a host cell line. There are many different methods available for transfecting mammalian cells, depending upon the cell line characteristics, desired effect, and downstream applications. These methods can be broadly divided into two categories: those used to generate transient transfection, and those used to generate stable transfectants. Transient transfection methods include, but are not limited to, liposome-mediated transfection, non-liposomal transfection agents (lipids and polymers), dendrimer-based transfection, and electroporation. Stable transfection methods include, but are not limited to microinjection, and virus-mediated gene delivery.

In certain aspects of the instant disclosure, stable transfection methods are used, *e.g.*, to achieve integration of exogenous, viral/VLP-forming genes into a mammalian cell genome. Such stable transfection approaches tend to rely upon homologous recombination to achieve directed integration of exogenous nucleic acid sequences, and are well known in the art.

Certain aspects of the instant disclosure describe methods and compositions designed to achieve delivery of exogenous viral genes to mammalian cells. Viral vectors, such as bacteriophages, retrovirus, adenovirus (types 2 and 5), adeno-associated virus, herpes virus, pox virus, human foamy virus (HFV), and lentivirus have been used for gene transfection. Viral vector genomes can be modified by deleting some areas of their genomes so that their replication becomes altered, rendering such viruses safer than native forms. However, viral delivery systems have some problems, including: the marked immunogenicity of viruses, which can cause induction of the inflammatory system, potentially leading to degeneration of transducted tissue; and toxin production, including mortality, the insertional mutagenesis; and their limitation in transgenic capacity size. During the past few years some viral vectors with specific receptors have been designed that are capable of transferring transgenes to some other specific cells, which are not their natural target cells (retargeting) (Nayerossadat *et al. Adv Biomed Res.* 1: 27).

Sequencing Methods

Some of the methods and compositions provided herein employ methods of sequencing nucleic acids. A number of DNA sequencing techniques are known in the art, including fluorescence-based sequencing methodologies (See, e.g., Birren et al, Genome Analysis Analyzing DNA, 1, Cold Spring Harbor, N.Y., which is incorporated herein by reference in its entirety). In some embodiments, automated sequencing techniques understood in that art are utilized. In some embodiments, parallel sequencing of partitioned amplicons can be utilized (PCT Publication No WO2006084132, which is incorporated herein by reference in its entirety). In some embodiments, DNA sequencing is achieved by parallel oligonucleotide extension (See, e.g., U.S. Pat. No. 5,750,341; U.S. Pat. No. 6,306,597, which are incorporated herein by reference in their entireties). Additional examples of sequencing techniques include the Church polony technology (Mitra et al, 2003, Analytical Biochemistry 320, 55-65; Shendure et al, 2005 Science 309, 1728- 1732; U.S. Pat. No. 6,432,360, U.S. Pat. No. 6,485,944, U.S. Pat. No. 6,511,803, which are incorporated by reference), the 454 picotiter pyrosequencing technology (Margulies et al, 2005 Nature 437, 376-380; US 20050130173, which are incorporated herein by reference in their entireties), the Solexa single base addition

technology (Bennett et al, 2005, Pharmacogenomics, 6, 373- 382; U.S. Pat. No. 6,787,308; U.S. Pat. No. 6,833,246, which are incorporated herein by reference in their entireties), the Lynx massively parallel signature sequencing technology (Brenner et al. (2000). Nat. Biotechnol. 18:630-634; U.S. Pat. No. 5,695,934; U.S. Pat. No. 5,714,330, which are incorporated herein by reference in their entireties), and the Adessi PCR colony technology (Adessi et al. (2000). Nucleic Acid Res. 28, E87; WO 00018957, which are incorporated herein by reference in their entireties).

Next-generation sequencing (NGS) methods can be employed in certain aspects of the instant disclosure to obtain a high volume of sequence information (such as are particularly required to perform deep sequencing VLPs following capture) in a highly efficient and cost effective manner. NGS methods share the common feature of massively parallel, high-throughput strategies, with the goal of lower costs in comparison to older sequencing methods (see, e.g., Voelkerding et al, Clinical Chem., 55: 641-658, 2009; MacLean et al, Nature Rev. Microbiol, 7- 287-296; which are incorporated herein by reference in their entireties). NGS methods can be broadly divided into those that typically use template amplification and those that do not. Amplification-utilizing methods include pyrosequencing commercialized by Roche as the 454 technology platforms (e.g., GS 20 and GS FLX), the Solexa platform commercialized by Illumina®, and the Supported Oligonucleotide Ligation and Detection (SOLiD™) platform commercialized by Applied Biosystems®. Non-amplification approaches, also known as single -molecule sequencing, are exemplified by the HeliScope platform commercialized by Helicos Biosciences, SMRT sequencing commercialized by Pacific Biosciences, and emerging platforms marketed by VisiGen and Oxford Nanopore Technologies Ltd.

In pyrosequencing (U.S. Pat. No. 6,210,891; U.S. Pat. No. 6,258,568, which are incorporated herein by reference in their entireties), template DNA is fragmented, end-repaired, ligated to adaptors, and clonally amplified in-situ by capturing single template molecules with beads bearing oligonucleotides complementary to the adaptors. Each bead bearing a single template type is compartmentalized into a water-in-oil microvesicle, and the template is clonally amplified using a technique referred to as emulsion PCR. The emulsion is disrupted after amplification and beads are deposited into individual wells of a picotitre plate functioning as a flow cell during the sequencing reactions. Ordered, iterative introduction of each of the four dNTP reagents occurs in the flow cell in the presence of sequencing enzymes and luminescent reporter such as luciferase. In the event that an appropriate dNTP is added to the 3' end of the sequencing primer, the resulting production of ATP causes a burst of luminescence

within the well, which is recorded using a CCD camera. It is possible to achieve read lengths greater than or equal to 400 bases, and 10^6 sequence reads can be achieved, resulting in up to 500 million base pairs (Mb) of sequence.

In the Solexa/Illumina platform (Voelkerding et al, Clinical Chem., 55- 641-658, 2009, MacLean et al, Nature Rev. Microbiol, 7:287-296; U.S. Pat. No. 6,833,246; U.S. Pat. No. 7,115,400; U.S. Pat. No. 6,969,488, which are incorporated herein by reference in their entireties), sequencing data are produced in the form of shorter-length reads. In this method, single-stranded fragmented DNA is end-repaired to generate 5'-phosphorylated blunt ends, followed by Klenow- mediated addition of a single A base to the 3' end of the fragments. A-addition facilitates addition of T-overhang adaptor oligonucleotides, which are subsequently used to capture the template-adaptor molecules on the surface of a flow cell that is studded with oligonucleotide anchors. The anchor is used as a PCR primer, but because of the length of the template and its proximity to other nearby anchor oligonucleotides, extension by PCR results in the "arching over" of the molecule to hybridize with an adjacent anchor oligonucleotide to form a bridge structure on the surface of the flow cell. These loops of DNA are denatured and cleaved. Forward strands are then sequenced with reversible dye terminators. The sequence of incorporated nucleotides is determined by detection of post- incorporation fluorescence, with each fluorophore and block removed prior to the next cycle of dNTP addition. Sequence read length ranges from 36 nucleotides to over 50 nucleotides, with overall output exceeding 1 billion nucleotide pairs per analytical run.

Sequencing nucleic acid molecules using SOLiD technology (Voelkerding et al, Clinical Chem., 55: 641-658, 2009; U.S. Patent No. 5,912,148; and U.S. Patent No. 6,130,073, which are incorporated herein by reference in their entireties) can initially involve fragmentation of the template, ligation to oligonucleotide adaptors, attachment to beads, and clonal amplification by emulsion PCR. Following this, beads bearing template are immobilized on a derivatized surface of a glass flow-cell, and a primer complementary to the adaptor oligonucleotide is annealed. However, rather than utilizing this primer for 3' extension, it is instead used to provide a 5' phosphate group for ligation to interrogation probes containing two probe- specific bases followed by 6 degenerate bases and one of four fluorescent labels. In the SOLiD system, interrogation probes have 16 possible combinations of the two bases at the 3' end of each probe, and one of four fluors at the 5' end. Fluor color, and thus identity of each probe, corresponds to specified color-space coding schemes. Multiple rounds (usually 7) of probe annealing, ligation, and fluor detection are followed by denaturation, and then a second round of sequencing using a primer that is offset by one base relative to the initial primer. In

this manner, the template sequence can be computationally re-constructed, and template bases are interrogated twice, resulting in increased accuracy. Sequence read length averages 35 nucleotides, and overall output exceeds 4 billion bases per sequencing run.

In certain embodiments, nanopore sequencing is employed (see, e.g., Astier et al, J. Am. Chem. Soc. 2006 Feb 8; 128(5): 1705-10, which is incorporated by reference). The theory behind nanopore sequencing has to do with what occurs when a nanopore is immersed in a conducting fluid and a potential (voltage) is applied across it. Under these conditions a slight electric current due to conduction of ions through the nanopore can be observed, and the amount of current is exceedingly sensitive to the size of the nanopore. As each base of a nucleic acid passes through the nanopore (or as individual nucleotides pass through the nanopore in the case of exonuclease-based techniques), this causes a change in the magnitude of the current through the nanopore that is distinct for each of the four bases, thereby allowing the sequence of the DNA molecule to be determined.

The Ion Torrent technology is a method of DNA sequencing based on the detection of hydrogen ions that are released during the polymerization of DNA (see, e.g., Science 327(5970): 1190 (2010); U.S. Pat. Appl. Pub. Nos. 20090026082, 20090127589, 20100301398, 20100197507, 20100188073, and 20100137143, which are incorporated herein by reference in their entireties). A microwell contains a template DNA strand to be sequenced. Beneath the layer of microwells is a hypersensitive ISFET ion sensor. All layers are contained within a CMOS semiconductor chip, similar to that used in the electronics industry. When a dNTP is incorporated into the growing complementary strand a hydrogen ion is released, which triggers a hypersensitive ion sensor. If homopolymer repeats are present in the template sequence, multiple dNTP molecules will be incorporated in a single cycle. This leads to a corresponding number of released hydrogens and a proportionally higher electronic signal. This technology differs from other sequencing technologies in that no modified nucleotides or optics are used. The per base accuracy of the Ion Torrent sequencer is approximately 99.6% for 50 base reads, with approximately 100 Mb generated per run. The read-length is 100 base pairs. The accuracy for homopolymer repeats of 5 repeats in length is approximately 98%. The benefits of ion semiconductor sequencing are rapid sequencing speed and low upfront and operating costs.

Kits

The instant disclosure also provides kits containing compositions of the instant disclosure, e.g., for use in methods of the present disclosure. Kits of the instant disclosure may

include one or more containers comprising a composition (e.g., a nucleic acid encoding for a virus like particle (VLP) producing protein and a nucleic acid encoding for an epitope-tagged viral surface protein, optionally further including an agent that binds the epitope) of this disclosure. In some embodiments, the kits further include instructions for use in accordance with the methods of this disclosure. In some embodiments, these instructions comprise a description of administration/transfection of the composition(s) to mammalian cells, optionally further including instructions for performance of isolation of VLPs and/or sequencing or other analysis of VLP-encapsulated cytosolic components (e.g., RNAs) produced by mammalian cell(s).

Instructions supplied in the kits of the instant disclosure are typically written instructions on a label or package insert (e.g., a paper sheet included in the kit), but machine-readable instructions (e.g., instructions carried on a magnetic or optical storage disk) are also acceptable. Instructions may be provided for practicing any of the methods described herein.

The kits of this disclosure are in suitable packaging. Suitable packaging includes, but is not limited to, vials, bottles, jars, flexible packaging (e.g., sealed Mylar or plastic bags), and the like. The container may further comprise a mammalian cell transfection agent.

Kits may optionally provide additional components such as buffers and interpretive information. Normally, the kit comprises a container and a label or package insert(s) on or associated with the container.

The practice of the present disclosure employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art. See, e.g., Maniatis et al., 1982, Molecular Cloning (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.), Sambrook et al., 1989, Molecular Cloning, 2nd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Sambrook and Russell, 2001, Molecular Cloning, 3rd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Ausubel et al., 1992), Current Protocols in Molecular Biology (John Wiley & Sons, including periodic updates); Glover, 1985, DNA Cloning (IRL Press, Oxford); Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988, Antibodies, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Jakoby and Pastan, 1979; Nucleic Acid Hybridization (B. D. Hames & S. J. Higgins eds. 1984); Transcription And Translation (B. D. Hames & S. J. Higgins eds. 1984); Culture Of Animal Cells (R. I. Freshney, Alan R. Liss, Inc., 1987); Immobilized Cells And Enzymes (IRL Press, 1986); B. Perbal, A Practical Guide To Molecular

Cloning (1984); the treatise, Methods In Enzymology (Academic Press, Inc., N.Y.); Gene Transfer Vectors For Mammalian Cells (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); Methods In Enzymology, Vols. 154 and 155 (Wu et al. eds.), Immunochemical Methods In Cell And Molecular Biology (Mayer and Walker, eds., Academic Press, London, 1987); Handbook Of Experimental Immunology, Volumes I- IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, Essential Immunology, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan et al., Manipulating the Mouse Embryo, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986); Westerfield, M., The zebrafish book. A guide for the laboratory use of zebrafish (Danio rerio), (4th Ed , Univ. of Oregon Press, Eugene, 2000).

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Reference will now be made in detail to exemplary embodiments of the disclosure. While the disclosure will be described in conjunction with the exemplary embodiments, it will be understood that it is not intended to limit the disclosure to those embodiments. To the contrary, it is intended to cover alternatives, modifications, and equivalents as may be included within the spirit and scope of the disclosure as defined by the appended claims. Standard techniques well known in the art or the techniques specifically described below were utilized.

EXAMPLES

Example 1: Materials and Methods

Nucleic Acid Sequences

The following nucleic acid sequences have been used in the instant disclosure:

CAG-Gag-GFP (SEQ ID NO: 24):

ACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCAT
AGCCCATATTGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTG
ACCGCCCAACGACCCCCGCCCCTTGACGTCAATAATGACGTATGTTCCCATAGTA
ACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTG
CCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGT
CAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGAC
TTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTGTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCA
AGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGG
ACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCG
TGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCC
TGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCC
AGCCTCCCCTCGAAGCTTTACATGTGGTACCGAGCTCGGATCCTGAGAACTTCAG
GGTGAGTCTATGGGACCCTTGATGTTTTCTTTCCCCTTCTTTTCTATGGTTAAGTTC
ATGTCATAGGAAGGGGAGAAGTAACAGGGTACACATATTGACCAAATCAGGGTA
ATTTTGCATTTGTAATTTTAAAAAATGCTTTCTTCTTTTAATATACTTTTTTGTTTA
TCTTATTTCTAATACTTTCCCTAATCTCTTTCTTTCAGGGCAATAATGATACAATG
TATCATGCCTCTTTGCACCATTCTAAAGAATAACAGTGATAATTTCTGGGTTAAG
GCAATAGCAATATTTCTGCATATAAATATTTCTGCATATAAATTGTAACTGATGT
AAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTATT
TTATGGTTGGGATAAGGCTGGATTATTCTGAGTCCAAGCTAGGCCCTTTTGCTAA
TCATGTTCATACCTCTTATCTTCCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGT
GTGCTGGCCCATCACTTTGGCAAAGAATTCgccaccATGGGCCAGACTGTTACCACT
CCCTTAAGTTTGACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACC
AGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCC
AACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAGACCTCATCACC
CAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACCAGGTCC
CCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGCC
CTTTGTACACCCTAAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCC
TTGAACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCT
TCTCTAGGCGCCAAACCTAAACCTCAAGTTCTTTCTGACAGTGGGGGGCCGCTCA
TCGACCTACTTACAGAAGACCCCCCGCCTTATAGGGACCCAAGACCACCCCCTTC
CGACAGGGACGGAAATGGTGGAGAAGCGACCCCTGCGGGAGAGGCACCGGACC
CCTCCCCAATGGCATCTCGCCTACGTGGGAGACGGGAGCCCCCTGTGGCCGACTC

CACTACCTCGCAGGCATTCCCCCTCCGCGCAGGAGGAAACGGACAGCTTCAATA
CTGGCCGTTCTCCTCTTCTGACCTTTACAACTGGAAAAATAATAACCCTTCTTTTT
CTGAAGATCCAGGTAAACTGACAGCTCTGATCGAGTCTGTCCTCATCACCCATCA
GCCCACCTGGGACGACTGTCAGCAGCTGTTGGGGACTCTGCTGACCGGAGAAGA
AAAACAACGGGTGCTCTTAGAGGCTAGAAAGGCGGTGCGGGGCGATGATGGGCG
CCCCACTCAACTGCCCAATGAAGTCGATGCCGCTTTTCCCCTCGAGCGCCCAGAC
TGGGATTACACCACCCAGGCAGGTAGGAACCACCTAGTCCACTATCGCCAGTTG
CTCCTAGCGGGTCTCCAAAACGCGGGCAGAAGCCCCACCAATTTGGCCAAGGTA
AAAGGAATAACACAAGGGCCCAATGAGTCTCCCTCGGCCTTCCTAGAGAGACTT
AAGGAAGCCTATCGCAGGTACACTCCTTATGACCCTGAGGACCCAGGGCAAGAA
ACTAATGTGTCTATGTCTTTCATTTGGCAGTCTGCCCCAGACATTGGGAGAAAGT
TAGAGAGGTTAGAAGATTTAAAAAACAAGACGCTTGGAGATTTGGTTAGAGAGG
CAGAAAAGATCTTTAATAAACGAGAAACCCCGGAAGAAAGAGAGGAACGTATC
AGGAGAGAAACAGAGGAAAAAGAAGAACGCCGTAGGACAGAGGATGAGCAGA
AAGAGAAAGAAAGAGATCGTAGGAGACATAGAGAGATGAGCAAGCTATTGGCC
ACTGTCGTTAGTGGACAGAAACAGGATAGACAGGGAGGAGAACGAAGGAGGTC
CCAACTCGATCGCGACCAGTGTGCCTACTGCAAAGAAAAGGGGCACTGGGCTAA
AGATTGTCCCAAGAAACCACGAGGACCTCGGGGACCAAGACCGCAGGGATCCGG
CGCAACAAACTTCTCTCTGCTGAAACAAGCCGGAGATGTCGAAGAGAATCCTGG
ACCGATGGAGAGCGACGAGAGCGGCCTGCCCGCCATGAAGATCGAGTGCCGCAT
CACCGGCACCCTGAACGGCGTGGAGTTCGAGCTGGTGGGCGGCGGAGAGGGCAC
CCCCGAGCAGGGCCGCATGACCAACAAGATGAAGAGCACCAAAGGCGCCCTGA
CCTTCAGCCCCTACCTGCTGAGCCACGTGATGGGCTACGGCTTCTACCACTTCGG
CACCTACCCCAGCGGCTACGAGAACCCCTTCCTGCACGCCATCAACAACGGCGG
CTACACCAACACCCGCATCGAGAAGTACGAGGACGGCGGCGTGCTGCACGTGAG
CTTCAGCTACCGCTACGAGGCCGGCCGCGTGATCGGCGACTTCAAGGTGGTGGG
CACCGGCTTCCCCGAGGACAGCGTGATCTTCACCGACAAGATCATCCGCAGCAA
CGCCACCGTGGAGCACCTGCACCCCATGGGCGATAACGTGCTGGTGGGCAGCTT
CGCCCGCACCTTCAGCCTGCGCGACGGCGGCTACTACAGCTTCGTGGTGGACAGC
CACATGCACTTCAAGAGCGCCATCCACCCCAGCATCCTGCAGAACGGGGGCCCC
ATGTTCGCCTTCCGCCGCGTGGAGGAGCTGCACAGCAACACCGAGCTGGGCATC
GTGGAGTACCAGCACGCCTTCAAGACCCCGGATGCAGATGCCGGTGAAGAA

CAG-FLAG-VSVG (K47A, R354A)-mCherry (SEQ ID NO: 25):

ACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCAT
AGCCCATATTGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTG
ACCGCCCAACGACCCCCGCCCCTTGACGTCAATAATGACGTATGTTCCCATAGTA
ACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTG
CCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGT
CAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGAC
TTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTGTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCA
AGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGG
ACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCG
TGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCC
TGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCC
AGCCTCCCCTCGAAGCTTTACATGTGGTACCGAGCTCGGATCCTGAGAACTTCAG
GGTGAGTCTATGGGACCCTTGATGTTTTCTTTCCCCTTCTTTTCTATGGTTAAGTTC
ATGTCATAGGAAGGGGAGAAGTAACAGGGTACACATATTGACCAAATCAGGGTA
ATTTTGCATTTGTAATTTTAAAAAATGCTTTCTTCTTTTAATATACTTTTTTGTTTA
TCTTATTTCTAATACTTTCCCTAATCTCTTTCTTTCAGGGCAATAATGATACAATG
TATCATGCCTCTTTGCACCATTCTAAAGAATAACAGTGATAATTTCTGGGTTAAG
GCAATAGCAATATTTCTGCATATAAATATTTCTGCATATAAATTGTAACTGATGT
AAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTATT
TTATGGTTGGGATAAGGCTGGATTATTCTGAGTCCAAGCTAGGCCCTTTTGCTAA
TCATGTTCATACCTCTTATCTTCCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGT
GTGCTGGCCCATCACTTTGGCAAAGAATTCgccaccATGAAGTGCCTTTTGTACTTA
GCCTTTTTATTCATTGGGGTGAATTGCAAGTTCACCATAGTTTTTCCATCCGGAGG
AGATTACAAGGATGACGACGATAAGGGCGGAAGCTTGGGACACAACCAAAAAG
GAAACTGGAAAAATGTTCCTTCTAATTACCATTATTGCCCGTCAAGCTCAGATTT
AAATTGGCATAATGACTTAATAGGCACAGCCTTACAAGTCAAAATGCCCGCGAG
TCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCATGCTTCCAAATGGGTCACT
ACTTGTGATTTCCGCTGGTATGGACCGAAGTATATAACACATTCCATCCGATCCT
TCACTCCATCTGTAGAACAATGCAAGGAAAGCATTGAACAAACGAAACAAGGAA
CTTGGCTGAATCCAGGCTTCCCTCCTCAAAGTTGTGGATATGCAACTGTGACGGA
TGCCGAAGCAGTGATTGTCCAGGTGACTCCTCACCATGTGCTGGTTGATGAATAC
ACAGGAGAATGGGTTGATTCACAGTTCATCAACGGAAAATGCAGCAATTACATA
TGCCCCACTGTCCATAACTCTACAACCTGGCATTCTGACTATAAGGTCAAAGGGC

TATGTGATTCTAACCTCATTTCCATGGACATCACCTTCTTCTCAGAGGACGGAGA
GCTATCATCCCTGGGAAAGGAGGGCACAGGGTTCAGAAGTAACTACTTTGCTTAT
GAAACTGGAGGCAAGGCCTGCAAAATGCAATACTGCAAGCATTGGGGAGTCAGA
CTCCCATCAGGTGTCTGGTTCGAGATGGCTGATAAGGATCTCTTTGCTGCAGCCA
GATTCCCTGAATGCCCAGAAGGGTCAAGTATCTCTGCTCCATCTCAGACCTCAGT
GGATGTAAGTCTAATTCAGGACGTTGAGAGGATCTTGGATTATTCCCTCTGCCAA
GAAACCTGGAGCAAAATCAGAGCGGGTCTTCCAATCTCTCCAGTGGATCTCAGCT
ATCTTGCTCCTAAAAACCCAGGAACCGGTCCTGCTTTCACCATAATCAATGGTAC
CCTAAAATACTTTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCAATCCTC
TCAAGAATGGTCGGAATGATCAGTGGAACTACCACAGAAGCGGAACTGTGGGAT
GACTGGGCACCATATGAAGACGTGGAAATTGGACCCAATGGAGTTCTGAGGACC
AGTTCAGGATATAAGTTTCCTTTATACATGATTGGACATGGTATGTTGGACTCCG
ATCTTCATCTTAGCTCAAAGGCTCAGGTGTTCGAACATCCTCACATTCAAGACGC
TGCTTCGCAACTTCCTGATGATGAGAGTTTATTTTTTGGTGATACTGGGCTATCCA
AAAATCCAATCGAGCTTGTAGAAGGTTGGTTCAGTAGTTGGAAAAGCTCTATTGC
CTCTTTTTTCTTTATCATAGGGTTAATCATTGGACTATTCTTGGTTCTCCGAGTTGG
TATCCATCTTTGCATTAAATTAAAGCACACCAAGAAAAGACAGATTTATACAGAC
ATAGAGATGAACCGACTTGGAAAGGAATTCGGATCCGGCGCAACAAACTTCTCT
CTGCTGAAACAAGCCGGAGATGTCGAAGAGAATCCTGGACCGatgGTGTCCAAGG
GCGAGGAAGATAACATGGCCATCATCAAGGAGTTCATGAGGTTTAAGGTCCACA
TGGAGGGTTCAGTCAATGGCCACGAGTTCGAGATTGAAGGCGAGGGCGAGGGCC
GCCCCTACGAAGGGACACAGACGGCGAAATTGAAGGTGACCAAAGGCGGGCCA
TTGCCCTTCGCATGGGACATCTTGTCCCCTCAGTTTATGTATGGCAGCAAGGCCT
ATGTTAAGCACCCCGCTGATATCCCGGACTACTTGAAGCTGTCCTTTCCAGAGGG
GTTTAAATGGGAGCGCGTTATGAATTTCGAAGACGGAGGAGTGGTTACGGTGAC
GCAGGACTCATCCCTGCAGGACGGAGAATTTATATATAAGGTTAAGTTGAGAGG
CACAAACTTCCCAAGCGACGGCCCTGTGATGCAGAAGAAAACAATGGGGTGGGA
AGCTTCCAGCGAGCGCATGTACCCCGAAGATGGCGCCCTCAAGGGCGAGATAAA
GCAAAGGCTGAAACTTAAGGACGGCGGTCATTACGACGCGGAGGTCAAGACAAC
TTACAAGGCTAAAAAACCCGTTCAGTTGCCTGGGGCTTACAATGTTAATATCAAA
CTTGACATCACAAGCCACAATGAAGACTATACGATCGTGGAGCAGTATGAACGA
GCGGAAGGCAGGCACTCAACGGGGGGGATGGACGAGCTTTACAAG

CAG-HA-VSVG (K47A, R354A)-mCherry (SEQ ID NO: 26):

ACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCAT
AGCCCATATTGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTG
ACCGCCCAACGACCCCCGCCCCTTGACGTCAATAATGACGTATGTTCCCATAGTA
ACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTG
CCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGT
CAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGAC
TTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTGTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCA
AGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGG
ACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCG
TGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCC
TGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCC
AGCCTCCCCTCGAAGCTTTACATGTGGTACCGAGCTCGGATCCTGAGAACTTCAG
GGTGAGTCTATGGGACCCTTGATGTTTTCTTTCCCCTTCTTTTCTATGGTTAAGTTC
ATGTCATAGGAAGGGGAGAAGTAACAGGGTACACATATTGACCAAATCAGGGTA
ATTTTGCATTTGTAATTTTAAAAAATGCTTTCTTCTTTTAATATACTTTTTTGTTTA
TCTTATTTCTAATACTTTCCCTAATCTCTTTCTTTCAGGGCAATAATGATACAATG
TATCATGCCTCTTTGCACCATTCTAAAGAATAACAGTGATAATTTCTGGGTTAAG
GCAATAGCAATATTTCTGCATATAAATATTTCTGCATATAAATTGTAACTGATGT
AAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTATT
TTATGGTTGGGATAAGGCTGGATTATTCTGAGTCCAAGCTAGGCCCTTTTGCTAA
TCATGTTCATACCTCTTATCTTCCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGT
GTGCTGGCCCATCACTTTGGCAAAGAATTCgccaccATGAAGTGCCTTTTGTACTTA
GCCTTTTTATTCATTGGGGTGAATTGCAAGTTCACCATAGTTTTTCCATCCGGAGG
ATACCCATACGATGTTCCAGATTACGCTGGCGGAAGCTTGGGACACAACCAAAA
AGGAAACTGGAAAAATGTTCCTTCTAATTACCATTATTGCCCGTCAAGCTCAGAT
TTAAATTGGCATAATGACTTAATAGGCACAGCCTTACAAGTCAAAATGCCCGCGA
GTCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCATGCTTCCAAATGGGTCAC
TACTTGTGATTTCCGCTGGTATGGACCGAAGTATATAACACATTCCATCCGATCC
TTCACTCCATCTGTAGAACAATGCAAGGAAAGCATTGAACAAACGAAACAAGGA
ACTTGGCTGAATCCAGGCTTCCCTCCTCAAAGTTGTGGATATGCAACTGTGACGG
ATGCCGAAGCAGTGATTGTCCAGGTGACTCCTCACCATGTGCTGGTTGATGAATA
CACAGGAGAATGGGTTGATTCACAGTTCATCAACGGAAAATGCAGCAATTACAT
ATGCCCCACTGTCCATAACTCTACAACCTGGCATTCTGACTATAAGGTCAAAGGG

CTATGTGATTCTAACCTCATTTCCATGGACATCACCTTCTTCTCAGAGGACGGAG
AGCTATCATCCCTGGGAAAGGAGGGCACAGGGTTCAGAAGTAACTACTTTGCTT
ATGAAACTGGAGGCAAGGCCTGCAAAATGCAATACTGCAAGCATTGGGGAGTCA
GACTCCCATCAGGTGTCTGGTTCGAGATGGCTGATAAGGATCTCTTTGCTGCAGC
CAGATTCCCTGAATGCCCAGAAGGGTCAAGTATCTCTGCTCCATCTCAGACCTCA
GTGGATGTAAGTCTAATTCAGGACGTTGAGAGGATCTTGGATTATTCCCTCTGCC
AAGAAACCTGGAGCAAAATCAGAGCGGGTCTTCCAATCTCTCCAGTGGATCTCA
GCTATCTTGCTCCTAAAAACCCAGGAACCGGTCCTGCTTTCACCATAATCAATGG
TACCCTAAAATACTTTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCAATC
CTCTCAAGAATGGTCGGAATGATCAGTGGAACTACCACAGAAGCGGAACTGTGG
GATGACTGGGCACCATATGAAGACGTGGAAATTGGACCCAATGGAGTTCTGAGG
ACCAGTTCAGGATATAAGTTTCCTTTATACATGATTGGACATGGTATGTTGGACT
CCGATCTTCATCTTAGCTCAAAGGCTCAGGTGTTCGAACATCCTCACATTCAAGA
CGCTGCTTCGCAACTTCCTGATGATGAGAGTTTATTTTTTGGTGATACTGGGCTAT
CCAAAAATCCAATCGAGCTTGTAGAAGGTTGGTTCAGTAGTTGGAAAAGCTCTAT
TGCCTCTTTTTTCTTTATCATAGGGTTAATCATTGGACTATTCTTGGTTCTCCGAGT
TGGTATCCATCTTTGCATTAAATTAAAGCACACCAAGAAAAGACAGATTTATACA
GACATAGAGATGAACCGACTTGGAAAGGAATTCGGATCCGGCGCAACAAACTTC
TCTCTGCTGAAACAAGCCGGAGATGTCGAAGAGAATCCTGGACCGatgGTGTCCA
AGGGCGAGGAAGATAACATGGCCATCATCAAGGAGTTCATGAGGTTTAAGGTCC
ACATGGAGGGTTCAGTCAATGGCCACGAGTTCGAGATTGAAGGCGAGGGCGAGG
GCCGCCCCTACGAAGGGACACAGACGGCGAAATTGAAGGTGACCAAAGGCGGG
CCATTGCCCTTCGCATGGGACATCTTGTCCCCTCAGTTTATGTATGGCAGCAAGG
CCTATGTTAAGCACCCCGCTGATATCCCGGACTACTTGAAGCTGTCCTTTCCAGA
GGGGTTTAAATGGGAGCGCGTTATGAATTTCGAAGACGGAGGAGTGGTTACGGT
GACGCAGGACTCATCCCTGCAGGACGGAGAATTTATATATAAGGTTAAGTTGAG
AGGCACAAACTTCCCAAGCGACGGCCCTGTGATGCAGAAGAAAACAATGGGGTG
GGAAGCTTCCAGCGAGCGCATGTACCCCGAAGATGGCGCCCTCAAGGGCGAGAT
AAAGCAAAGGCTGAAACTTAAGGACGGCGGTCATTACGACGCGGAGGTCAAGAC
AACTTACAAGGCTAAAAAACCCGTTCAGTTGCCTGGGGCTTACAATGTTAATATC
AAACTTGACATCACAAGCCACAATGAAGACTATACGATCGTGGAGCAGTATGAA
CGAGCGGAAGGCAGGCACTCAACGGGGGGGATGGACGAGCTTTACAAG

Transfections were carried out using Lipofectamine® 2000, following manufacturer's instructions. Transductions were carried out by transducing cells with lentivirus carrying transgenes, and then selection was performed either using antibiotics (such as puromycin) or by flow cytometry (if using a fluorescent protein such as GFP). VLPs were harvested from media and then purified by centrifuging at 2000 rcf for 10 minutes at 4 °C, then filtering the supernatant with a 0.45 μm cellulose acetate filter. The VLPs were optionally further concentrated *via* ultracentrifugation (using a 20% sucrose cushion) or using a 100k MWCF (such as an amicon filter) and centrifuging for 4000 rcf for 30 minutes at 4 °C. The concentrated VLPs were optionally further purified *via* immunoprecipitation with appropriate beads (such as Anti-FLAG M2 magnetic beads) and following manufacturer's instructions. RNAseq was carried out using SMART-Seq.

Example 2: Induction of Mammalian Cell Production of Epitope-Tagged VLPs

In retroviruses, VLPs have been described as generated by endogenous or ectopic expression of gag or gag-like proteins. Recognizing that VLPs encapsulate cytosolic components of their originating cells, including proteins, lipids, metabolites, small molecules, RNA and/or DNA (see FIGs. 1A and 1B), it was first examined whether VLP formation could be induced in mammalian cells. Once induced, it was contemplated herein that VLPs could then be specifically isolated as a means of measuring transcriptome expression levels in living cells in real time/across a time course. For purification of VLPs, it was examined whether VLPs could be tagged (e.g., *via* introduction of epitope tags such as HA, FLAG, etc.), thereby allowing for immunoprecipitation (IP) or other affinity-based methods to isolate VLPs (i.e. via IP of cell line-specific and/or virion-specific tags; FIG. 1D). In addition or as an alternative, it was also contemplated that VLPs could be isolated via centrifugation, concentration *via* molecular weight cutoff filters, gradients, crowding agents (such as PEG), or a combination of the aforementioned methods. It was contemplated herein that the VLPs produced by a mammalian cell harboring a VLP producing protein could be isolated and used to assess a variety of mammalian cell analytes in real time/across a time course, while maintaining an intact and alive mammalian cell throughout such a monitoring period. Further, it was specifically contemplated that VLPs could be isolated and used to assess RNA as the mammalian cell analyte tracked in real-time/across a time course and at high throughput, via application of Next Generation Sequencing (NGS) technologies to such isolated populations of VLPs (FIG. 1E). It was projected that expression profiling results could be determined over

time from the same biological sample(s) via transcriptome-directed assessment of VLPs (FIG. 1F).

Example 3: Epitope-Tagged VLPs Provided High Quality RNA Libraries

Nucleic acids encoding for a retroviral gag protein (specifically, MLV gag) and a flag epitope-tagged envelope protein (here, flag-VSV-g) were introduced into mammalian 293T cells. Immunoprecipitation was performed upon the flag epitope tag, and western blot results confirmed that gag protein could be specifically and cleanly isolated via epitope-mediated IP from supernatant, which confirmed that VLPs were successfully isolated (FIG. 2A). VLP samples were then sequenced for RNA content, and dot plot data of supernatants obtained from conditions where MLV gag was transfected demonstrated that the instant approach generated high quality RNA libraries, as measured by genes detected (which confirmed both the depth and diversity of the VLP-derived RNA libraries; FIG. 2B). Background from VLPs lacking flag-labeled envelopes was identified as negligible (FIG. 2D).

Example 4: Distinct Epitope Tags Readily Distinguished Cell Lines of Origin, Even in Mixed Cell Culture

To examine whether different mammalian cell lines of origin could provide real-time/time course analyte information that was independently identifiable as attributable to VLPs generated by respective types of mammalian cell lines, two distinct cell lines (here, 293T cells and HT1080) were administered retroviral gag and either flag epitope-labeled envelope (flag-VSV-G) constructs or HA epitope-labeled envelope constructs (HA-VSV-G). As shown in FIGs. 3A and 3B, populations of VLPs from each cell type could be readily distinguished at the transcriptome/genes detected level, based upon the respective epitope tags used correlating with depth of sequence coverage obtained. Specifically, high quality transcript libraries (quantified by genes detected at sequencing) were generated when each supernatant was put through the matching immunoprecipitation step. Conversely, poor quality transcript (RNAseq) libraries (quantified by genes detected) were generated when each supernatant was put through an incorrect (unmatched) immunoprecipitation (FIG. 3B).

It was next examined if mixed cell populations presenting distinct epitope tags on their VLP envelope proteins (thereby distinguishing their respective VLPs at origin, before mixing) could be identified in co-culture based upon these epitope tags. As shown in FIG. 4, epitope tag-isolated VLPs were readily distinguished as reflecting their cell type of origin (here, 293T or HT1080), even when obtained from a mixed cellular population in culture.

Additional transcript sequencing (RNAseq) data also confirmed that quantitative transcriptional information could be measured from live-cell co-cultures via purification of affinity-tagged VLPs *via* immunoprecipitation (FIG. 5), as demonstrated by the extensive correlation observed between assays.

Example 5: Transcriptome Monitoring of Living Cells in Co-Culture and in Model Systems

The compositions and methods of the instant disclosure can be employed to provide significant insight in *in vitro* screens with complex cell populations, where RNA information is desired from each sub-population of cells. Populations can be independently modified with the constructs, and subsequently pooled together, or specific promoters can be used to specifically label desired populations. A specifically contemplated example of such a system is an *in vitro* screen performed upon primary cortical neurons, such as E18 rat or mouse cortical neurons. Such cultures contain several cell types, such as excitatory neurons, inhibitory neurons and glia. In certain aspects, to examine the effects of perturbations in such cells caused by small molecules, siRNA/shRNA, CRISPRi/a, gene knockout (via CRISPR or other methods), metabolites, viruses, proteins, peptides, photons (with or without optogenetics), ORFs, prokaryotes, or other eukaryotic cells, optionally during screening, the following compositions and methods are employed. Successful labeling of VLPs from excitatory neurons is performed by using a CamKII promoter to drive expression of both a VLP producing protein, such as MLV Gag, as well as a labeled envelope protein, such as FLAG-VSVG. Meanwhile, successful labeling of VLPs from inhibitory neurons is performed using a mDlx promoter to drive expression of both a VLP producing protein, such as MLV Gag, as well as a labeled envelope protein, such as HA-VSVG. In this example, these subpopulations are simultaneously modified by delivering constructs driven by these cell-type specific promoters via AAV (optionally together with adenovirus), lentivirus, or transfection. Particles are collected by sampling the supernatant, performing a 2000 rcf centrifugation for 10 minutes at 4 °C, and then incubating in the appropriate immunoprecipitation or affinity beads and performing the capture and elution per manufacturer's instructions. After the elution of the particles, RNA sequencing (optionally by RNAseq), mass spectrometry, western blot, northern blot, microarray, luminex, droplet based library construction (such as 10x single cell 3'), or other detection method, is performed.

The instant disclosure is also contemplated as providing significant insight in an animal model where cells are modified with the constructs of the disclosure *ex vivo* and then subsequently implanted. An example of this is a cancer model in mice, where *ex vivo* modified

gag+ flag-vsvg+ luciferase+ HT1080 cells or 293T cells are administered *via* intraperitoneal injection. Cell invasion and metastasis can be monitored via luciferase detection using standard methods, and this cellular behavior can be coupled with VLP-derived analyte (e.g., transcriptome sequences, e.g., RNAseq) information *via* blood sampling such as sampling via tail vein. The resulting samples can be processed using affinity capture and then analyte assessment (e.g., RNAseq) can be performed. In this example, *in vivo* metastasis information can optionally be coupled with analyte assessment (e.g., RNAseq) information, in order to better assess and understand mechanisms of metastasis *in vivo*.

The compositions and methods of the instant disclosure can also provide significant insight in an animal model where cells are modified with the constructs *in vivo*. For example, the constructs described herein can be packaged in AAV with a modified capsid that permits blood brain barrier crossing, such as AAV-PHP.B. This AAV can be delivered *via* intravenous injection, thus modifying neurons directly *in vivo*. To examine the transcriptomes of different neuronal cell-types *in vivo*, cerebral spinal fluid can be collected and processed, selecting the exported particles via affinity capture and elution. After the elution of the particles, VLP-captured analyte assessement vie transcriptome detection (*e.g.*, via RNAseq), mass spectrometry, western blot, northern blot, microarray, luminex, droplet based library construction (such as 10x single cell 3'), can be performed, in order to couple freely-behaving animal observations such as development, behavior and/or *in vivo* perturbations with high-throughput molecular readouts.

A strength of the compositions and methods of the instant disclosure is that the compositions and methods can be used to monitor broad transcriptional information, rather than focus on a few genes. The methods are particularly well suited for cases where cells are implanted/modified *in vivo*, or are non-dividing *in vitro*. One particularly interesting expressly contemplated use case is an engineered patient-derived xenografts (PDX) model for glioblastoma multiforme (GBM) in immunodeficient mice. Using an approach of the instant disclosure, transcriptional responses from CSF are gathered after administering different small molecules or biologics possessing potential therapeutic impact. The transcriptional data are used to measure gene expression across all gene ontologies of interest, which include cell cycle regulation, apoptosis, stemness/pluripotency, and/or differentiation. Further, since the instant compositions and methods capture full-length transcriptional information, mutations can be

identified and mechanisms of resistance can be deciphered as therapeutic pressure is strengthened in a particular animal model.

Thus, expressly contemplated applications for the compositions and methods of the instant disclosure include *in vitro* studies of complex cellular populations (such as primary cortical neurons, which have excitatory neurons, inhibitory neurons, glia and other cell types, as described in additional detail above), and assessment of implanted cells (such as cancerous cells) in animal models (in the case of studying implanted cells in animal models, it is contemplated that cells are optionally infected *ex vivo* before implantation or are infected *in vivo*/*in situ*, e.g., *via* viral or other directed modes of gene delivery *in vivo*), with VLP-captured analytes (e.g., transcription changes) then monitored as VLP-producing cells invade or proliferate in such animal models, and/or as agents (*e.g.*, candidate drugs) are administered to the animal model.

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the disclosure pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

One skilled in the art would readily appreciate that the present disclosure is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the disclosure. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the disclosure, are defined by the scope of the claims.

In addition, where features or aspects of the disclosure are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the disclosure is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

The use of the terms "a" and "an" and "the" and similar referents in the context of describing the disclosure (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms "comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range,

unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein.

All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the disclosure and does not pose a limitation on the scope of the disclosure unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the disclosure.

Embodiments of this disclosure are described herein, including the best mode known to the inventors for carrying out the disclosed invention. Variations of those embodiments may become apparent to those of ordinary skill in the art upon reading the foregoing description.

The disclosure illustratively described herein suitably can be practiced in the absence of any element or elements, limitation or limitations that are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of", and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present disclosure provides preferred embodiments, optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this disclosure as defined by the description and the appended claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications can be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present disclosure and the following claims. The present disclosure teaches one skilled in the art to test various combinations and/or substitutions of chemical modifications described herein toward generating conjugates possessing improved contrast, diagnostic and/or imaging activity. Therefore, the specific embodiments described herein are not limiting and one skilled in the art can readily appreciate that specific combinations of the modifications described herein can be tested without undue experimentation toward identifying conjugates possessing improved contrast, diagnostic and/or imaging activity.

The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the disclosure to be practiced otherwise than as specifically described herein. Accordingly, this disclosure includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the disclosure unless otherwise indicated herein or otherwise clearly contradicted by context. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure described herein. Such equivalents are intended to be encompassed by the following claims.

We Claim:

1. A mammalian cell comprising a virus like particle (VLP) producing protein and an epitope-tagged viral surface protein.

2. A mammalian cell comprising an epitope-tagged virus like particle (VLP) producing protein.

3. A mammalian cell comprising a virus like particle (VLP) producing protein and a viral surface protein of a virus differing from the virus of the virus like particle (VLP) producing protein.

4. The mammalian cell of claim 2 or claim 3, wherein the VLP is a non-enveloped virus VLP, optionally wherein the non-enveloped virus comprises an engineered affinity tag, optionally wherein the non-enveloped virus VLP is selected from the group consisting of an *Adenoviridae*, a *Papovaviridae*, a *Parvoviridae*, and an *Anelloviridae* family virus.

5. The mammalian cell of any one of claims 1-4, wherein the virus like particle (VLP) producing protein is a retroviral gag protein or a viral gag-like protein, optionally wherein the viral gag protein is selected from the group consisting of a murine leukemia virus (MLV) gag protein, a retrovirus matrix protein, a rhabdovirus matrix (M) protein (optionally VSVM protein), a filovirus viral core protein (optionally an Ebola VP40 viral protein), a Rift Valley Fever virus N protein (optionally RVFV N Protein having GenBank serial number NP049344), a coronavirus M, E and/or NP protein (optionally GenBank serial number NP040838 for NP protein, GenBank serial number NP 040835 for M protein, GenBank serial number CAC39303 for E protein of Avian Infections Bronchitis Virus and GenBank serial number NP828854 for E protein of the SARS virus), a bunyavirus N protein (optionally the bunyavirus N protein of GenBank serial number AAA47114), an influenza M1 protein, a paramyxovirus M protein, an arenavirus Z protein (optionally a Lassa Fever Virus Z protein), an AAV gag-like protein (optionally selected from the group consisting of AAV1 capsid, AAV2 capsid, AAV3 capsid, AAV4 capsid, AAV5 capsid, AAV6 capsid, AAV7 capsid, AAV8 capsid, AAV9 capsid, AAV10 capsid, AAV11 capsid, AAV12 capsid, and AAV13 capsid), and combinations thereof.

6. The mammalian cell of claim 1, wherein the epitope-tagged viral surface protein is a Vesicular Stomatitis Virus (VSV) glycoprotein (VSV-G) or a mutagenized form of VSV-G,

optionally wherein the mutagenized form of VSV-G prevents VSV-G-mediated cellular uptake.

7. The mammalian cell of claim 1, wherein the epitope-tagged viral surface protein is an epitope-tagged viral envelope protein, optionally wherein the epitope-tagged viral envelope protein is selected from the group consisting of an epitope-tagged form of any of the following: a Vesicular Stomatitis Virus (VSV) glycoprotein, a retrovirus glycoprotein (optionally a human immunodeficiency virus (HIV) envelope glycoprotein (optionally HIVSF162 envelope glycoprotein of GenBank serial number M65024)), a simian immunodeficiency virus (SIV) envelope glycoprotein (optionally SIVmac239 envelope glycoprotein of GenBank serial number M33262), a simian-human immunodeficiency virus (SHIV) envelope glycoprotein (optionally SHIV-89.6p envelope glycoprotein of GenBank serial number U89134), a feline immunodeficiency virus (FIV) envelope glycoprotein (optionally FIV envelope glycoprotein of GenBank serial number L00607), a feline leukemia virus (FLV) envelope glycoprotein (optionally the FLV envelope glycoprotein of GenBank serial number M12500), a bovine immunodeficiency virus (BIV) envelope glycoprotein (optionally the BIV envelope glycoprotein of GenBank serial number NC001413), a bovine leukemia virus (BLV) envelope glycoprotein (optionally of GenBank serial number AF399703), an equine infectious anemia virus envelope glycoprotein (optionally the equine infectious anemia virus envelope glycoprotein of GenBank serial number NC001450), a human T-cell leukemia virus envelope glycoprotein (optionally the human T-cell leukemia virus envelope glycoprotein of GenBank serial number AF0033817), a mouse mammary tumor virus envelope glycoprotein (MMTV), a bunyavirus glycoprotein (optionally a Rift Valley Fever virus (RVFV) glycoprotein (optionally the RVFV envelope glycoprotein of GenBank serial number M11157)), an arenavirus glycoprotein (optionally a Lassa fever virus glycoprotein (optionally of GenBank serial number AF333969))), a filovirus glycoprotein (e.g., an Ebola virus glycoprotein (GenBank serial number NC002549)), a corona virus glycoprotein (optionally of GenBank serial number SARS coronavirus spike protein AAP13567), an influenza virus glycoprotein (optionally of GenBank serial number V01085), a paramyxovirus glycoprotein (optionally of GenBank serial number NC002728 for Nipah virus F and G proteins), a rhabdovirus glycoprotein (optionally of GenBank serial number NP049548)), an alphavirus glycoprotein (optionally of GenBank serial number AAA48370 for Venezuelan equine encephalomyelitis (VEE)), a flavivirus glycoprotein (optionally of GenBank serial number NC001563 for West

Nile virus and/or a Hepatitis C Virus glycoprotein), a Herpes Virus glycoprotein (optionally a cytomegalovirus glycoprotein), and combinations thereof.

8. The mammalian cell of claim 1, wherein the epitope-tagged viral surface protein is selected from the group consisting of Coronavirus gpE1, Coronavirus Peplomer Protein E1, Coronavirus Peplomer Protein E2 JHM, Hepatitis Virus (MHV), Glycoprotein E2, LaCrosse Virus Envelope Glycoprotein G1, Simian Sarcoma Virus Glycoprotein 70, Viral Envelope Glycoprotein gp55 (Friend Virus), and Viral Envelope Glycoprotein gPr90 (Murine Leukemia Virus).

9. The mammalian cell of any one of claims 1 and 5-8, wherein the epitope tag is selected from the group consisting of FLAG (DYKDDDDK; SEQ ID NO: 3), 6 x His (HHHHHH; SEQ ID NO: 4), HA (YPYDVPDYA; SEQ ID NO: 5), c-myc (EQKLISEEDL; SEQ ID NO: 6), V5 tag (GKPIPNPLLGLDST; SEQ ID NO: 7), AU1 tag (DTYRYI; SEQ ID NO: 8), AU5 tag (TDFYLK; SEQ ID NO: 9), Glu-Glu tag (EYMPME; SEQ ID NO: 10), OLLAS (SGFANELGPRLMGK; SEQ ID NO. 11), T7 tag (MASMTGGQQMG; SEQ ID NO: 12), VSV-G tag (YTDIEMNRLGK; SEQ ID NO: 13), E-Tag (GAPVPYPDPLEPR; SEQ ID NO: 14), S-Tag (KETAAAKFERQHMDS; SEQ ID NO: 15), HSV tag (SQPELAPEDPED; SEQ ID NO: 16), KT3 tag (KPPTPPPEPET; SEQ ID NO: 17), TK15 tag, GST tag, Protein A tag, CD tag, Strep-Tag (WSHPQFEK; SEQ ID NO: 18), MBP tag, CBD tag, Avi tag (CGLNDIFEAQKIEWHE; SEQ ID NO: 19), CBP tag, TAP tag, and SF-TAP tag.

10. The mammalian cell of any one of claims 1-9, wherein the mammalian cell is infected by a virus, optionally wherein the mammalian cell is infected by AAV (and optionally adenovirus, HPV or other virus), or by a retrovirus, optionally wherein the retrovirus is a lentivirus.

11. The mammalian cell of any one of claims 1-10, wherein the mammalian cell is a cell in culture.

12. The mammalian cell of any one of claims 1-11, wherein the mammalian cell is a neuronal cell, optionally a primary cortical neuron, optionally an excitatory neuron or an inhibitory neuron.

13. The mammalian cell of any one of claims 1-12, wherein the mammalian cell is a cell *in vivo*.

14. The mammalian cell of any one of claims 1-13, wherein the VLP producing protein and/or the epitope-tagged viral surface protein are produced by the mammalian cell *via* a genomically integrated nucleic acid sequence that encodes for the VLP producing protein and/or the epitope-tagged viral surface protein, optionally wherein the nucleic acid sequence that encodes for the VLP producing protein and/or the epitope-tagged viral surface protein is under the control of a mammalian promoter, optionally a CMV promoter, a SV40 promoter and/or a tissue-specific mammalian promoter (optionally a mDlx, CamKII, Syn1, NSE, PDGF and/or Ta1 promoter, optionally a CamKII promoter and/or a mDlx promoter).

15. A method for obtaining an expression profile of a living cell, the method comprising:

(a) providing a living cell;

(b) introducing a nucleic acid sequence encoding for a VLP producing protein to the living cell, wherein introduction of the nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cell;

(c) isolating VLPs produced by the living cell *via* binding of a VLP protein; and

(d) performing RNA sequencing upon the isolated VLPs, thereby obtaining expression profile information for the isolated VLPs, wherein the expression profile information for the isolated VLPs reflects the expression profile of the living cell,

thereby obtaining an expression profile of the living cell.

16. The method of claim 15, wherein the VLP protein of step (c) is the VLP producing protein, optionally wherein the VLP producing protein is tagged, optionally wherein the tag is an epitope tag.

17. The method of claim 15 or claim 16, wherein the VLP is a non-enveloped virus VLP, optionally wherein the non-enveloped virus comprises an engineered affinity tag, optionally wherein the non-enveloped virus VLP is selected from the group consisting of an *Adenoviridae*, a *Papovaviridae*, a *Parvoviridae*, and an *Anelloviridae* family virus.

18. The method of any one of claims 15-17, wherein the VLP protein of step (c) is a capsid protein of the VLP or an envelope protein of the VLP.

19. The method of any one of claims 15 or 17-18, wherein the VLP protein of step (c) is a host cell membrane protein, optionally an affinity-tagged host cell membrane protein.

20. The method of claim 18, wherein the capsid protein of the VLP or the envelope protein of the VLP is tagged, optionally wherein the tag is an epitope tag.

21. The method of any one of claims 15-20, wherein an antibody is used to bind the VLP protein in step (c).

22. The method of claim 21, wherein the antibody binds the VLP producing protein, a capsid protein of the VLP, and/or an envelope protein of the VLP.

23. The method of claim 16 or claim 20, wherein the epitope tag is selected from the group consisting of FLAG (DYKDDDDK; SEQ ID NO: 3), 6 x His (HHHHHH; SEQ ID NO: 4), HA (YPYDVPDYA; SEQ ID NO: 5), c-myc (EQKLISEEDL; SEQ ID NO: 6), V5 tag (GKPIPNPLLGLDST; SEQ ID NO: 7), AU1 tag (DTYRYI; SEQ ID NO: 8), AU5 tag (TDFYLK; SEQ ID NO: 9), Glu-Glu tag (EYMPME; SEQ ID NO: 10), OLLAS (SGFANELGPRLMGK; SEQ ID NO: 11), T7 tag (MASMTGGQQMG; SEQ ID NO: 12), VSV-G tag (YTDIEMNRLGK; SEQ ID NO: 13), E-Tag (GAPVPYPDPLEPR; SEQ ID NO: 14), S-Tag (KETAAAKFERQHMDS; SEQ ID NO: 15), HSV tag (SQPELAPEDPED; SEQ ID NO: 16), KT3 tag (KPPTPPPEPET; SEQ ID NO: 17), TK15 tag, GST tag, Protein A tag, CD tag, Strep-Tag (WSHPQFEK; SEQ ID NO: 18), MBP tag, CBD tag, Avi tag (CGLNDIFEAQKIEWHE; SEQ ID NO: 19), CBP tag, TAP tag, and SF-TAP tag.

24. The method of any one of claims 15-23, wherein the virus like particle (VLP) producing protein is a retroviral gag protein or a viral gag-like protein, optionally wherein the viral gag protein is selected from the group consisting of a murine leukemia virus (MLV) gag protein, a retrovirus matrix protein, a rhabdovirus matrix (M) protein (optionally VSVM protein), a filovirus viral core protein (optionally an Ebola VP40 viral protein), a Rift Valley Fever virus N protein (optionally RVFV N Protein having GenBank serial number NP049344), a coronavirus M, E and/or NP protein (optionally GenBank serial number NP040838 for NP protein, GenBank serial number NP 040835 for M protein, GenBank serial number CAC39303 for E protein of Avian Infections Bronchitis Virus and GenBank serial number NP828854 for E protein of the SARS virus), a bunyavirus N protein (optionally the bunyavirus N protein of GenBank serial number AAA47114), an influenza M1 protein, a paramyxovirus M protein, an arenavirus Z protein (optionally a Lassa Fever Virus Z protein), an AAV gag-like protein (optionally selected from the group consisting of AAV1 capsid, AAV2 capsid, AAV3 capsid, AAV4 capsid, AAV5 capsid, AAV6 capsid, AAV7 capsid,

AAV8 capsid, AAV9 capsid, AAV10 capsid, AAV11 capsid, AAV12 capsid, and AAV13 capsid), and combinations thereof.

25. A method for obtaining an expression profile of a living cell, the method comprising:

(a) providing a living cell;

(b) introducing a first nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid encoding for an epitope-tagged viral surface protein to the living cell, wherein introduction of the first nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cell;

(c) isolating VLPs produced by the living cell *via* binding of the epitope-tagged viral surface protein; and

(d) performing RNA sequencing upon the isolated VLPs, thereby obtaining expression profile information for the isolated VLPs, wherein the expression profile information for the isolated VLPs reflects the expression profile of the living cell,

thereby obtaining an expression profile of the living cell.

26. The method of claim 25, wherein the virus like particle (VLP) producing protein is a retroviral gag protein or a viral gag-like protein, optionally wherein the viral gag protein is selected from the group consisting of a murine leukemia virus (MLV) gag protein, a retrovirus matrix protein, a rhabdovirus matrix (M) protein (optionally VSVM protein), a filovirus viral core protein (optionally an Ebola VP40 viral protein), a Rift Valley Fever virus N protein (optionally RVFV N Protein having GenBank serial number NP049344), a coronavirus M, E and/or NP protein (optionally GenBank serial number NP040838 for NP protein, GenBank serial number NP 040835 for M protein, GenBank serial number CAC39303 for E protein of Avian Infections Bronchitis Virus and GenBank serial number NP828854 for E protein of the SARS virus), a bunyavirus N protein (optionally the bunyavirus N protein of GenBank serial number AAA47114), an influenza M1 protein, a paramyxovirus M protein, an arenavirus Z protein (optionally a Lassa Fever Virus Z protein), an AAV gag-like protein (optionally selected from the group consisting of AAV1 capsid, AAV2 capsid, AAV3 capsid, AAV4 capsid, AAV5 capsid, AAV6 capsid, AAV7 capsid, AAV8 capsid, AAV9 capsid, AAV10 capsid, AAV11 capsid, AAV12 capsid, and AAV13 capsid), and combinations thereof.

27. The method of claim 25 or claim 26, wherein the epitope-tagged viral surface protein is a Vesicular Stomatitis Virus (VSV) glycoprotein (VSV-G) or a mutagenized form of VSV-

G, optionally wherein the mutagenized form of VSV-G prevents VSV-G-mediated cellular uptake.

28. The method of any one of claims 25-27, wherein the epitope-tagged viral surface protein is an epitope-tagged viral envelope protein, optionally wherein the epitope-tagged viral envelope protein is selected from the group consisting of an epitope-tagged form of any of the following: a Vesicular Stomatitis Virus (VSV) glycoprotein, a retrovirus glycoprotein (optionally a human immunodeficiency virus (HIV) envelope glycoprotein (optionally HIVSF162 envelope glycoprotein of GenBank serial number M65024)), a simian immunodeficiency virus (SIV) envelope glycoprotein (optionally SIVmac239 envelope glycoprotein of GenBank serial number M33262), a simian-human immunodeficiency virus (SHIV) envelope glycoprotein (optionally SHIV-89.6p envelope glycoprotein of GenBank serial number U89134), a feline immunodeficiency virus (FIV) envelope glycoprotein (optionally FIV envelope glycoprotein of GenBank serial number L00607), a feline leukemia virus (FLV) envelope glycoprotein (optionally the FLV envelope glycoprotein of GenBank serial number M12500), a bovine immunodeficiency virus (BIV) envelope glycoprotein (optionally the BIV envelope glycoprotein of GenBank serial number NC001413), a bovine leukemia virus (BLV) envelope glycoprotein (optionally of GenBank serial number AF399703), an equine infectious anemia virus envelope glycoprotein (optionally the equine infectious anemia virus envelope glycoprotein of GenBank serial number NC001450), a human T-cell leukemia virus envelope glycoprotein (optionally the human T-cell leukemia virus envelope glycoprotein of GenBank serial number AF0033817), a mouse mammary tumor virus envelope glycoprotein (MMTV), a bunyavirus glycoprotein (optionally a Rift Valley Fever virus (RVFV) glycoprotein (optionally the RVFV envelope glycoprotein of GenBank serial number M11157)), an arenavirus glycoprotein (optionally a Lassa fever virus glycoprotein (optionally of GenBank serial number AF333969))), a filovirus glycoprotein (e.g., an Ebola virus glycoprotein (GenBank serial number NC002549)), a corona virus glycoprotein (optionally of GenBank serial number SARS coronavirus spike protein AAP13567), an influenza virus glycoprotein (optionally of GenBank serial number V01085), a paramyxovirus glycoprotein (optionally of GenBank serial number NC002728 for Nipah virus F and G proteins), a rhabdovirus glycoprotein (optionally of GenBank serial number NP049548)), an alphavirus glycoprotein (optionally of GenBank serial number AAA48370 for Venezuelan equine encephalomyelitis (VEE)), a flavivirus glycoprotein (optionally of GenBank serial number NC001563 for West Nile virus and/or a Hepatitis C Virus

glycoprotein), a Herpes Virus glycoprotein (optionally a cytomegalovirus glycoprotein), and combinations thereof.

29. The method of any one of claims 25-28, wherein the epitope-tagged viral surface protein is selected from the group consisting of Coronavirus gpE1, Coronavirus Peplomer Protein E1, Coronavirus Peplomer Protein E2 JHM, Hepatitis Virus (MHV), Glycoprotein E2, LaCrosse Virus Envelope Glycoprotein G1, Simian Sarcoma Virus Glycoprotein 70, Viral Envelope Glycoprotein gp55 (Friend Virus), and Viral Envelope Glycoprotein gPr90 (Murine Leukemia Virus).

30. The method of any one of claims 25-29, wherein the epitope tag of the epitope-tagged viral surface protein is selected from the group consisting of FLAG (DYKDDDDK; SEQ ID NO: 3), 6 x His (HHHHHH; SEQ ID NO: 4), HA (YPYDVPDYA; SEQ ID NO: 5), c-myc (EQKLISEEDL; SEQ ID NO: 6), V5 tag (GKPIPNPLLGLDST; SEQ ID NO: 7), AU1 tag (DTYRYI; SEQ ID NO: 8), AU5 tag (TDFYLK; SEQ ID NO: 9), Glu-Glu tag (EYMPME; SEQ ID NO: 10), OLLAS (SGFANELGPRLMGK; SEQ ID NO: 11), T7 tag (MASMTGGQQMG; SEQ ID NO: 12), VSV-G tag (YTDIEMNRLGK; SEQ ID NO: 13), E-Tag (GAPVPYPDPLEPR; SEQ ID NO: 14), S-Tag (KETAAAKFERQHMDS; SEQ ID NO: 15), HSV tag (SQPELAPEDPED; SEQ ID NO: 16), KT3 tag (KPPTPPPEPET; SEQ ID NO: 17), TK15 tag, GST tag, Protein A tag, CD tag, Strep-Tag (WSHPQFEK; SEQ ID NO: 18), MBP tag, CBD tag, Avi tag (CGLNDIFEAQKIEWHE; SEQ ID NO: 19), CBP tag, TAP tag, and SF-TAP tag.

31. The method of any one of claims 25-30, wherein the living cell is infected by a virus, optionally wherein the living cell is infected by AAV (and optionally adenovirus, HPV or other virus), or by a retrovirus, optionally wherein the retrovirus is a lentivirus.

32. The method of any one of claims 25-31, wherein the living cell is a mammalian cell, optionally a mammalian cell in culture.

33. The method of any one of claims 25-32, wherein the living cell is a neuronal cell, optionally a primary cortical neuron, optionally an excitatory neuron or an inhibitory neuron.34. The method of any one of claims 25-33, wherein the living cell is a cell *in vivo*, optionally a living cell in a mouse model of disease, optionally a living cell in an engineered patient-derived xenograft (PDX) model for glioblastoma multiforme (GBM).

35. The method of any one of claims 23-33, wherein the living cell is a living cell in a rat, optionally a primary rat cortical neurons or a primary rat hippocampal neuron, optionally obtained from microsurgically dissected tissue, optionally from a E18 Sprague Dawley rat.

36. The method of any one of claims 25-35, wherein the first nucleic acid sequence and the second nucleic acid sequence are present on the same nucleic acid construct.

37. The method of any one of claims 25-35, wherein the first nucleic acid sequence and the second nucleic acid sequence are present on different nucleic acid constructs.

38. The method of any one of claims 25-74, wherein the first nucleic acid sequence and/or the second nucleic acid sequence are genomically integrated.

39. The method of any one of claims 25-38, wherein the VLP producing protein and/or the epitope-tagged viral surface protein is under the control of a mammalian promoter, optionally a CMV promoter, a SV40 promoter and/or a tissue-specific mammalian promoter (optionally a mDlx, CamKII, Syn1, NSE, PDGF and/or Ta1 promoter, optionally a CamKII promoter and/or a mDlx promoter).

40. A method for obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells, the method comprising:

(a) providing a first population of living cells;

(b) introducing a first nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid encoding for a first epitope-tagged viral surface protein to the first population of living cells, wherein introduction of the first nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the first population of living cells;

(c) providing a second population of living cells;

(d) introducing the first nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid sequence encoding for a second epitope-tagged viral surface protein to the second population of living cells, wherein introduction of the first nucleic acid sequence comprising a nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the second population of living cells;

(e) isolating VLPs produced by the first population of living cells *via* binding of the first epitope-tagged viral surface protein;

(f) obtaining a first analyte profile from the isolated VLPs of the first population of living cells;

(g) isolating VLPs produced by the second population of living cells *via* binding of the second epitope-tagged viral surface protein; and

(h) obtaining a second analyte profile from the isolated VLPs of the second population of living cells,

thereby obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells.

41. A method for obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells, the method comprising:

(a) providing a first population of living cells;

(b) introducing a first nucleic acid sequence encoding for a VLP producing protein to the first population of living cells, wherein introduction of the first nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the first population of living cells;

(c) providing a second population of living cells;

(d) introducing a second nucleic acid sequence encoding for a VLP producing protein to the second population of living cells, wherein introduction of the second nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the second population of living cells;

(e) isolating VLPs produced by the first population of living cells *via* binding of a first VLP protein;

(f) obtaining a first analyte profile from the isolated VLPs of the first population of living cells;

(g) isolating VLPs produced by the second population of living cells *via* binding of a second VLP protein; and

(h) obtaining a second analyte profile from the isolated VLPs of the second population of living cells,

thereby obtaining a first analyte profile for a first population of living cells and a second analyte profile for a second population of living cells.

42. The method of claim 41, wherein the first VLP protein is specific to the first population of cells and the second VLP protein is specific to the second population of cells, optionally

wherein the first VLP protein is the VLP producing protein encoded by the first nucleic acid and/or the second VLP protein is the VLP producing protein encoded by the second nucleic acid.

43. The method of claim 41 or claim 42, wherein the binding of isolating step (e) is performed using an antibody and/or the binding of isolating step (g) is performed using an antibody.

44. The method of any one of claims 41-43, wherein the first VLP protein and/or the second VLP protein is tagged, optionally epitope-tagged.

45. The method of any one of claims 41-44, wherein the analyte profile comprises transcript information.

46. A method for assessing a test compound for efficacy and/or toxicity in living cells, the method comprising:

(a) providing a population of living cells;

(b) introducing a nucleic acid sequence encoding for a VLP producing protein to the living cells, wherein introduction of the nucleic acid sequence encoding for the VLP producing protein is sufficient to induce budding of VLPs from the living cells;

(c) contacting the living cells with a test compound;

(d) isolating VLPs produced by the living cells *via* binding of a VLP protein; and

(e) obtaining analyte profile information from the isolated VLPs, wherein the analyte profile information indicates the efficacy and/or toxicity of the test compound,

thereby assessing a test compound for efficacy and/or toxicity in living cells.

47. A method for assessing a test compound for efficacy and/or toxicity in living cells, the method comprising:

(a) providing a population of living cells,

(b) introducing a first nucleic acid sequence encoding for a VLP producing protein and a second nucleic acid sequence encoding for an epitope-tagged viral surface protein to the living cells, wherein introduction of the nucleic acid sequence encoding for a VLP producing protein is sufficient to induce budding of VLPs from the living cells;

(c) contacting the living cells with a test compound;

(d) isolating VLPs produced by the living cells *via* binding of the epitope-tagged viral surface protein; and

(e) obtaining analyte profile information from the isolated VLPs, wherein the analyte profile information indicates the efficacy and/or toxicity of the test compound,

thereby assessing a test compound for efficacy and/or toxicity in living cells.

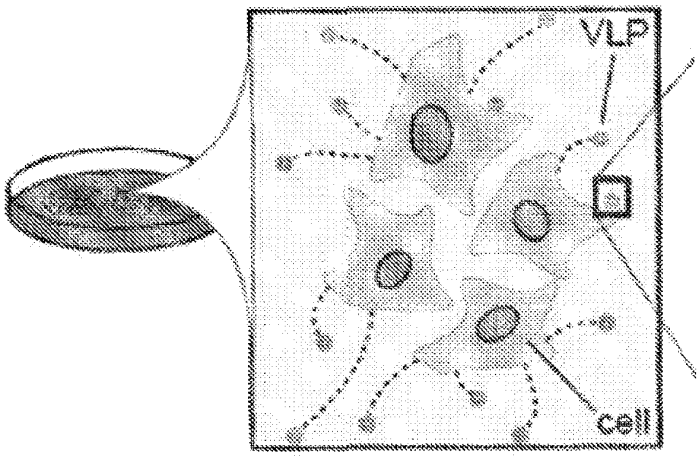


FIG. 1A

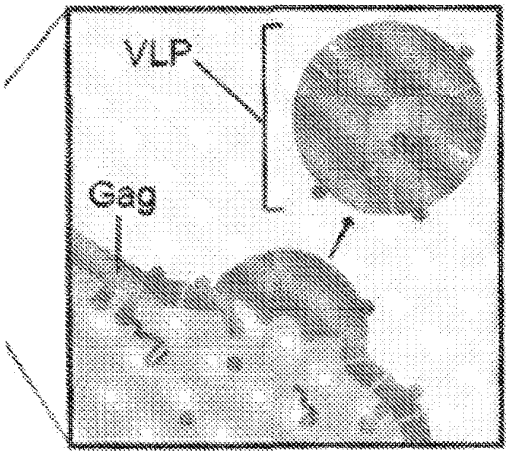


FIG. 1B

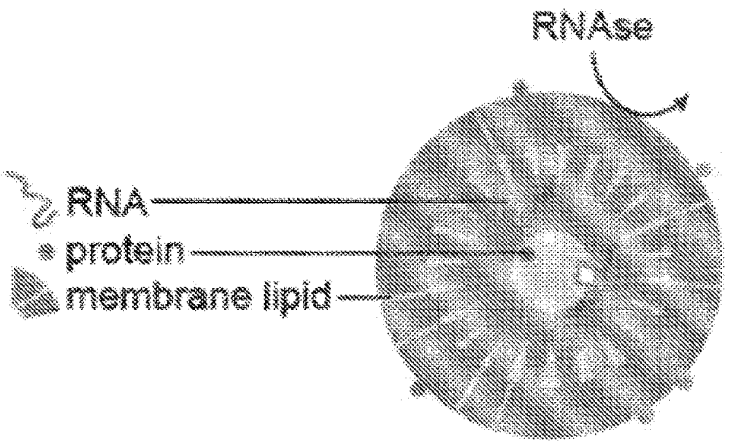

RNAse
RNA
protein
membrane lipid

FIG. 1C

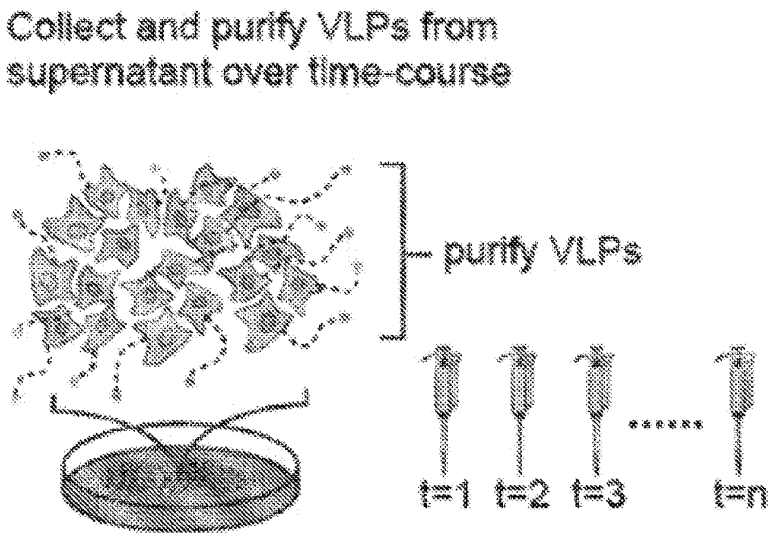

Collect and purify VLPs from supernatant over time-course
purify VLPs
t=1
t=2
t=3
t=n

FIG. 1D

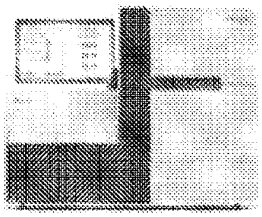


FIG. 1E

1

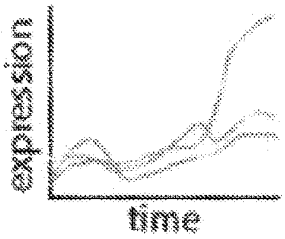


FIG. 1F

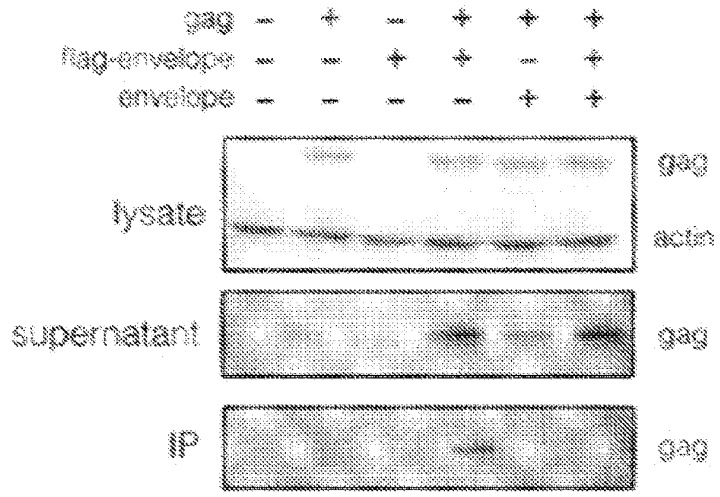

gag
flag-envelope
envelope
lysate
supernatant
IP
gag
actin
gag
gag

FIG. 2A

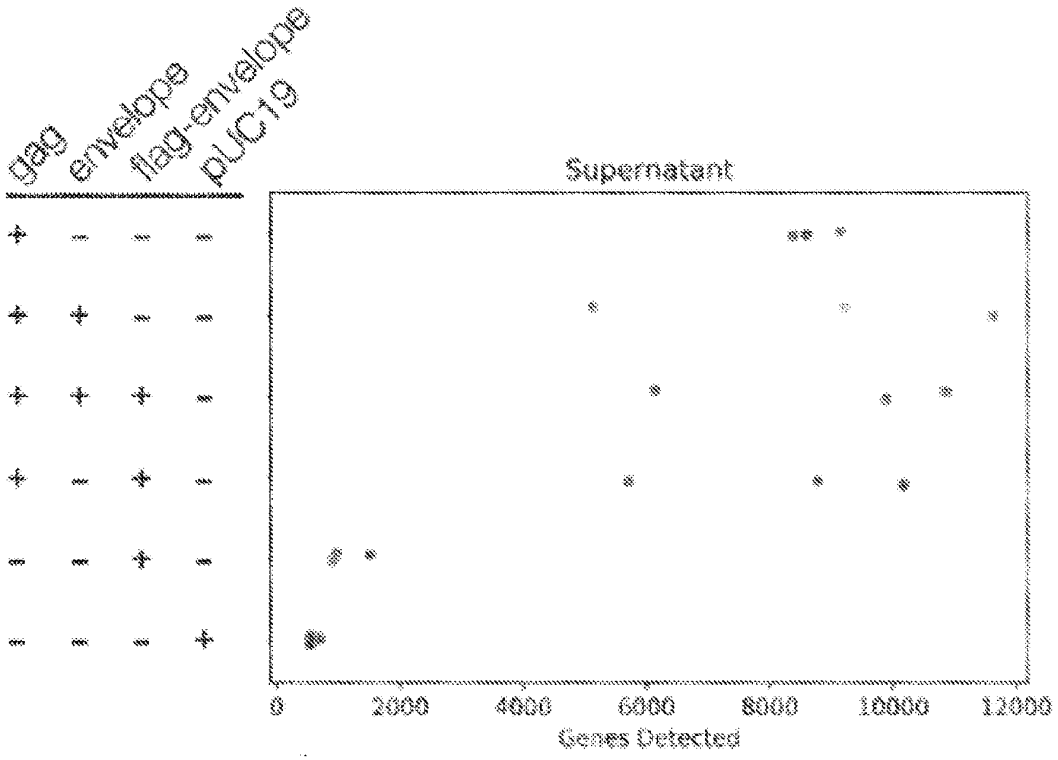

gag
envelope
flag-envelope
pUC19
Supernatant
0
2000
4000
6000
8000
10000
12000
Genes Detected

FIG. 2B

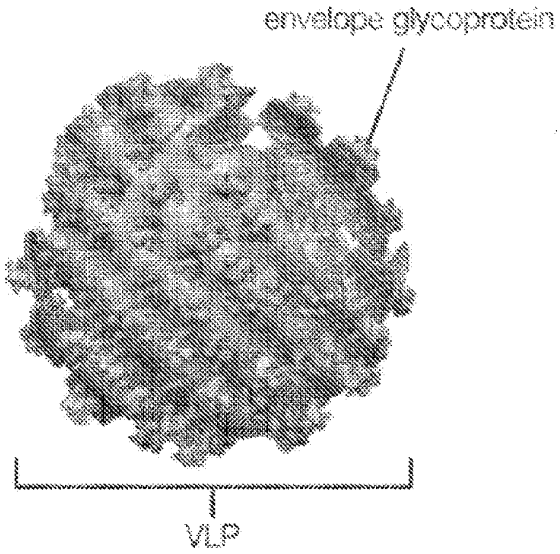

envelope glycoprotein
VLP

FIG. 2C

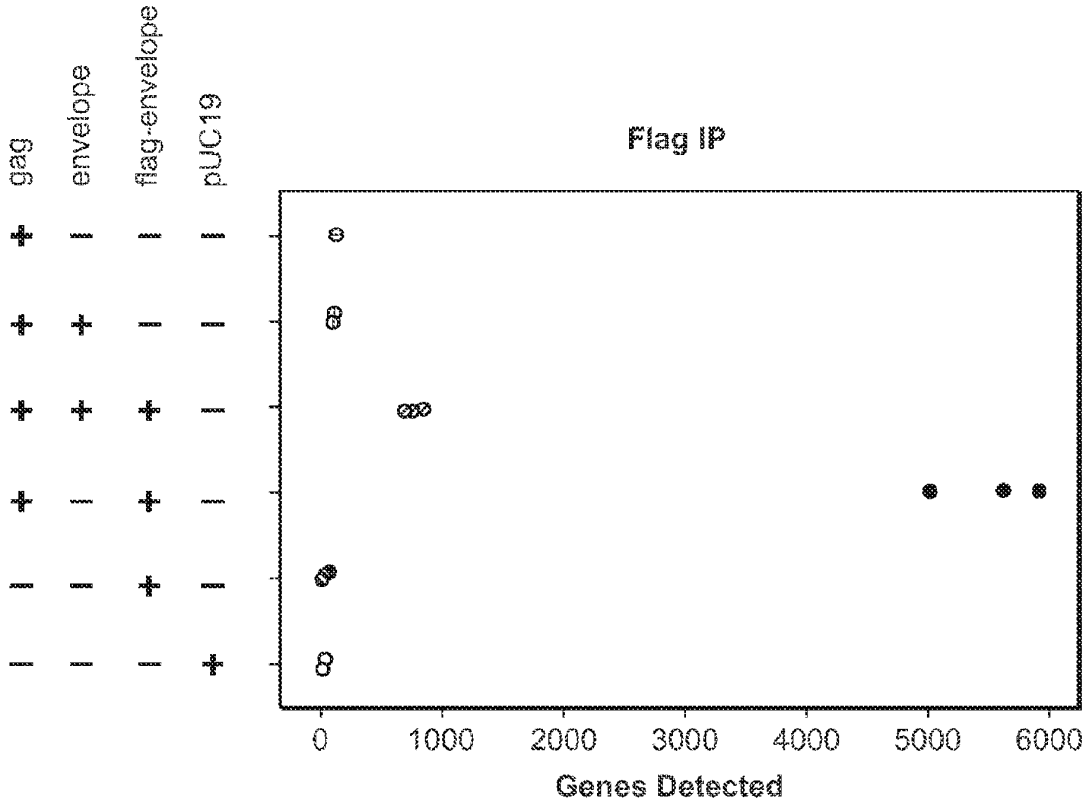

gag
envelope
flag-envelope
pUC19
Flag IP
0
1000
2000
3000
4000
5000
6000
Genes Detected

FIG. 2D

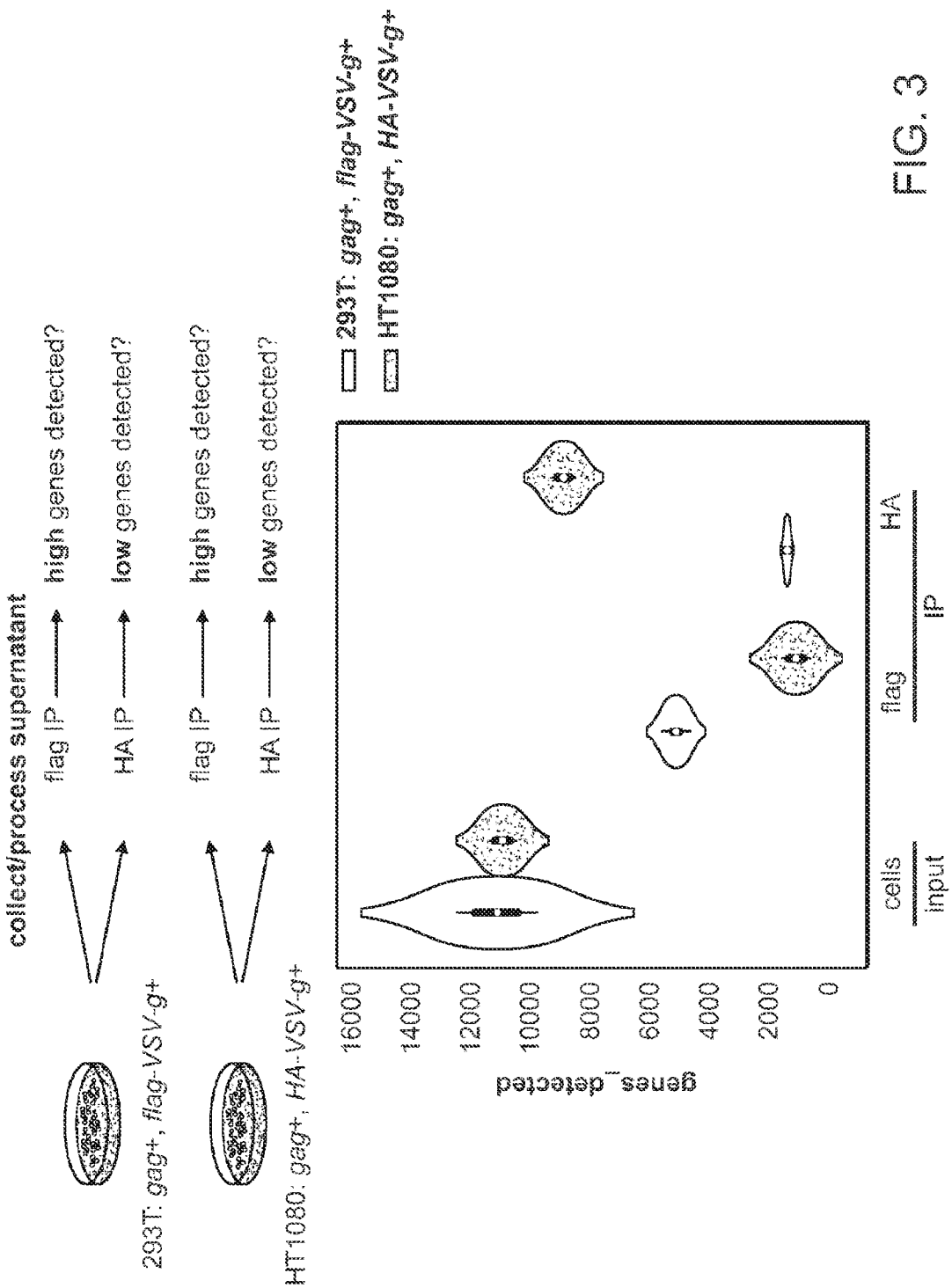

collect/process supernatant
flag IP
high genes detected?
HA IP
low genes detected?
293T: gag+, flag-VSV-g+
flag IP
high genes detected?
HA IP
low genes detected?
HT1080: gag+, HA-VSV-g+
293T: gag+, flag-VSV-g+
HT1080: gag+, HA-VSV-g+
genes_detected
16000
14000
12000
10000
8000
6000
4000
2000
0
cells
input
flag
HA
IP

FIG. 3

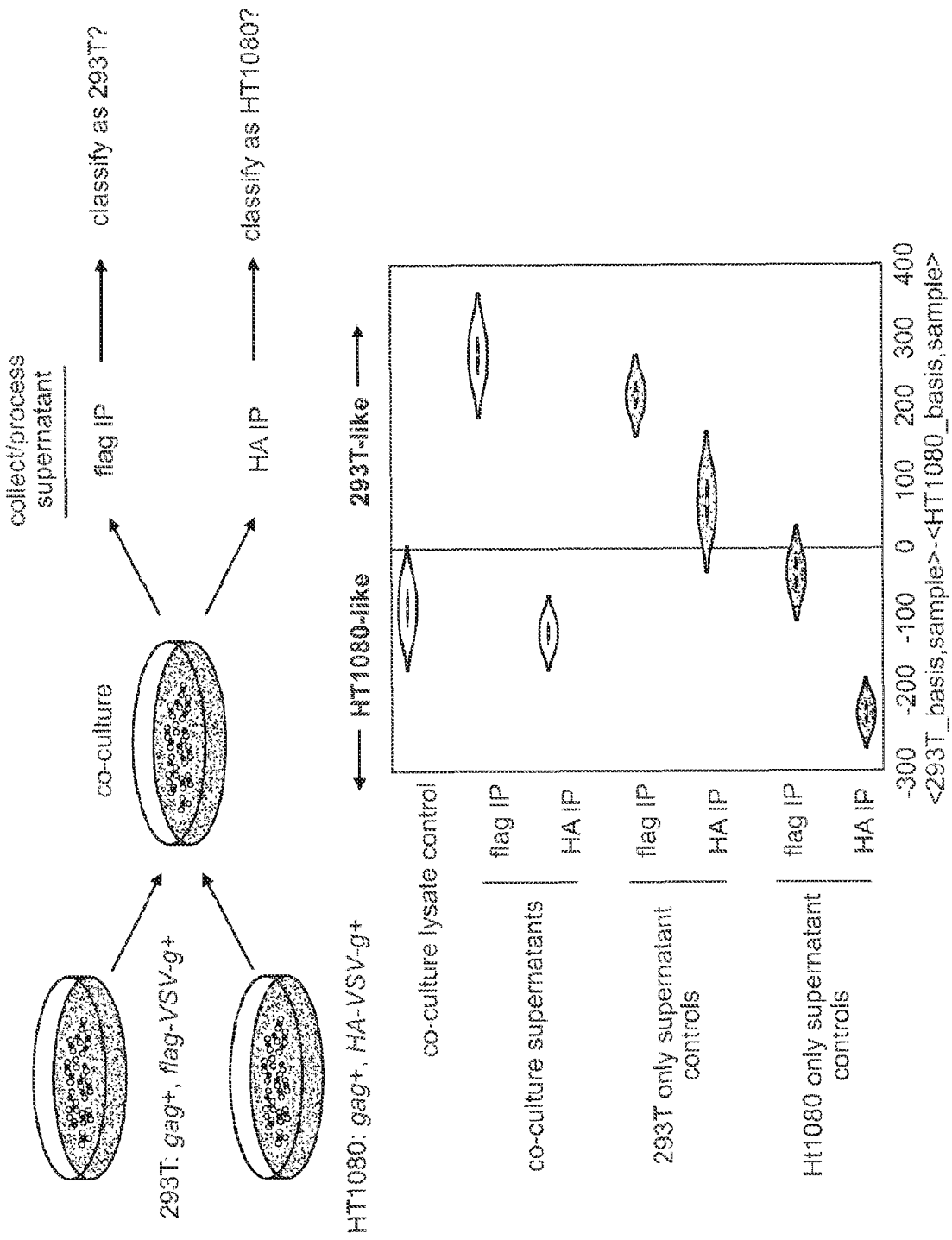

collect/process supernatant
flag IP
classify as 293T?
HA IP
classify as HT1080?
co-culture
293T: gag+, flag-VSV-g+
HT1080: gag+, HA-VSV-g+
HT1080-like
293T-like
co-culture lysate control
co-culture supernatants
flag IP
HA IP
293T only supernatant controls
flag IP
HA IP
Ht1080 only supernatant controls
flag IP
HA IP
-300 -200 -100 0 100 200 300 400
<293T_basis,sample>-<HT1080_basis,sample>

FIG. 4

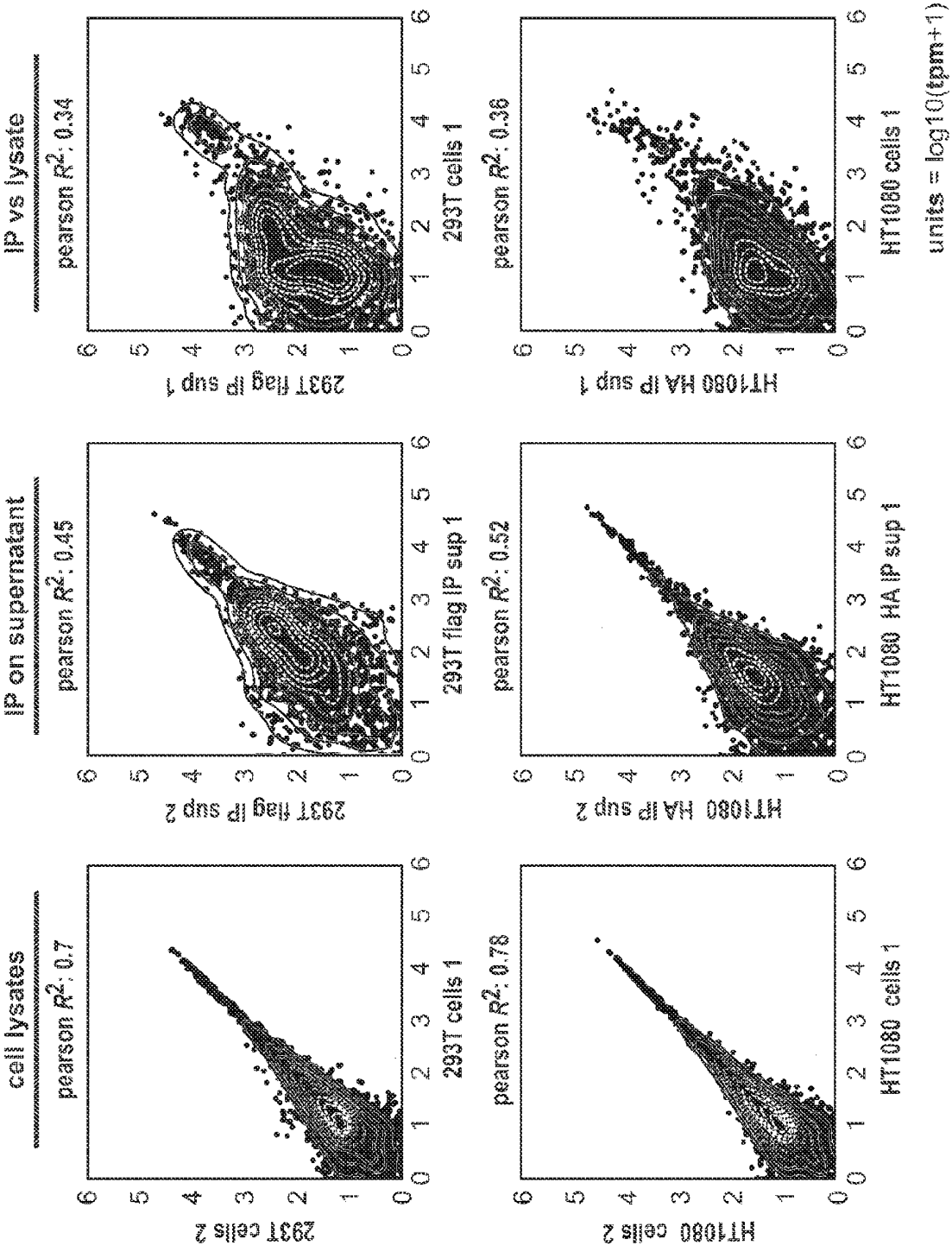

cell lysates
pearson R^2: 0.7
293T cells 1
293T cells 2
IP on supernatant
pearson R^2: 0.45
293T flag IP sup 1
293T flag IP sup 2
IP vs lysate
pearson R^2: 0.34
293T flag IP sup 1
pearson R^2: 0.78
HT1080 cells 1
HT1080 cells 2
pearson R^2: 0.52
HT1080 HA IP sup 1
HT1080 HA IP sup 2
pearson R^2: 0.36
HT1080 cells 1
HT1080 HA IP sup 1
units = log10(tpm+1)

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2020/030286

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/12; A61K 39/21; C07K 14/005; C07K 14/16; C12N 7/04; C12N 15/10 (2020.01)
CPC - A61K 39/21; C07K 14/005; C07K 14/16; C12N 7/04; C12N 15/1065; C12N 2740/16023; C12N 2740/16222; C12Q 1/6844; C12Q 1/6874 (2020.05)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
see Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
see Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
see Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/0079786 A1 (THE BROAD INSTITUTE, INC. et al) 22 March 2018 (22.03.2018) entire document	1-4, 7, 8, 15-17, 25, 26, 40-43
Y		5, 27, 46, 47
Y	US 2019/0119335 A1 (CHILDREN'S MEDICAL CENTER CORPORATION) 25 April 2019 (25.04.2019) entire document	6, 27
Y	US 2016/0122753 A1 (MIKKELSEN et al) 05 May 2016 (05.05.2016) entire document	46, 47
A	LEE et al. "High-Throughput Drug Screening Using the Ebola Virus Transcription- and Replication-Competent Virus-Like Particle System," Antiviral Research, 01 October 2018 (01.10.2018), Vol. 158, Pgs. 226-237. entire document	1-4, 6-8, 15-17, 25-27, 40-43, 46, 47
A	US 2018/0045719 A1 (VIB VZW et al) 15 February 2018 (15.02.2018) entire document	1-4, 6-8, 15-17, 25-27, 40-43, 46, 47

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 June 2020	03 AUG 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2020/030286

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 5, 9-14, 18-24, 28-39, 44, 45
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2020/030286

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☒ furnished subsequent to the international filing date for the purposes of international search only:

      ☒ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a))

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**06/28/2023 04:13:57 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Julianne Holland
PATENT CENTER #	62352719	AUTHORIZED BY	Christopher Bodle
CUSTOMER #	51414	FILING DATE	12/15/2022
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Ronnie M. Russell

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 1146	E20236RG15197806	Julianne Holland

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2202	EACH CLAIM IN EXCESS OF 20	40.00	7	280.00
			TOTAL AMOUNT:	**$280.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: INH-014
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ronnie M. Russell et al.

Application No.: 18/066,420 | Confirmation No.: 1909

Filed: December 15, 2022 | Art Unit: 1633

For: PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF | Examiner: BURKHART, MICHAEL D

INFORMATION DISCLOSURE STATEMENT (IDS)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs:

Pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98, the attention of the United States Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of the above-identified application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed more than three months after the filing date of this application, OR more than three months after the date of entry of the national stage in the international application, AND after the mailing date of a first Office Action on the merits, but before the mailing date of any of a Final Action under 37 C.F.R. § 1.113, a Notice of Allowance under 37 C.F.R. § 1.311 or an action that otherwise closes prosecution in this application (37 C.F.R. § 1.97(c)).

Pursuant to 37 C.F.R. § 1.97(e)(1), each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office

in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), copies of U.S. patents and U.S. patent application publications are not submitted. Submitted herewith are copies of foreign patents and non-patent literature in accordance with 37 C.F.R. § 1.98(a)(2).

A concise explanation of relevance of the non-English references listed on form PTO/SB/08 is given for each listed item.

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 07-1700, under Order No. INH-014 from which the undersigned is authorized to draw.

Dated: June 28, 2023

Respectfully submitted,

Electronic signature: /Christopher R. Bodle/
Christopher R. Bodle, Ph.D.
Registration No.: 80,876
GOODWIN PROCTER LLP
100 Northern Avenue
IP DOCKETING DEPT./7TH FL
Boston, Massachusetts 02210
(617) 570-1000
Attorney/Agent For Applicant

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 18/066,420	Filing Date 12/15/2022	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

	(Column 1)	(Column 2)			
FOR	NUMBER FILED	NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $50 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $240 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/VICTOR BARLOW/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

51414 7590 07/26/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 07/26/2023

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

TITLE OF INVENTION: PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	10/26/2023

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

51414 7590 07/26/2023
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

TITLE OF INVENTION: PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0.00	$0.00	$480	10/26/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
BURKHART, MICHAEL D	1633	424-130100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via Patent Center or EFS-Web ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

51414 7590 07/26/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 07/26/2023

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 18/066,420	Applicant(s) Russell et al.	
	Examiner MICHAEL D BURKHART	Art Unit 1633	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to the response dated 6/28/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 76-83 and 85-106 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☑ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 6/28/2023.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☑ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MICHAEL D BURKHART/
Primary Examiner, Art Unit 1633

EXAMINER'S AMENDMENT

Double Patenting

The rejection of certain claims on the grounds of nonstatutory double patenting over application 18/157,421 is withdrawn in light of amendment of the claims.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: the prior art does not teach or suggest VSV-G envelope proteins (SEQ ID NO: 2) comprising the recited I182E or I182D substitution mutations. The closest relevant art is represented by Kim et al (US 20210106632 A1), which teaches the VSV-G envelope protein comprising substitutions at residue 162.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL D BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached M-F 8-5.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Babic can be reached on 571 272-8507. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available

to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL D BURKHART/
Primary Examiner, Art Unit 1633

Notice of References Cited	Application/Control No. 18/066,420	Applicant(s)/Patent Under Reexamination Russell et al.	
	Examiner MICHAEL D BURKHART	Art Unit 1633	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20210106632-A1	04-2021	KIM; Gi-Beom	A61K9/0019	1/1
	B					1/1
	C					
	D					1/1
	E					1/1
	E					1/1
	G					
	H					1/1
	I					1/1
	J					1/1
	K					1/1
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	H					1/1
	O					1/1
	P					
	O					1/1
	R					1/1
	S					
	I					1/1

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/066,420	Russell et al.
	Examiner	**Art Unit**
	MICHAEL D BURKHART	1633

CPC							
Symbol						**Type**	**Version**
C07K	/	16	/	2896		F	2013-01-01
C12N	/	15	/	113		I	2013-01-01
C12N	/	15	/	113		I	2013-01-01
C12N	/	2740	/	15043		A	2013-01-01

CPC Combination Sets								
Symbol						**Type**	**Set**	**Ranking**	**Version**
	/		/						

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	30	
/MICHAEL D BURKHART/ Primary Examiner, Art Unit 1633	15 July 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20230715

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/066,420	Russell et al.
	Examiner	Art Unit
	MICHAEL D BURKHART	1633

INTERNATIONAL CLASSIFICATION					
CLAIMED					
C12N	/	15	/	15	
NON-CLAIMED					
	/		/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	30	
/MICHAEL D BURKHART/ Primary Examiner, Art Unit 1633	15 July 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20230715

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/066,420	Russell et al.
	Examiner	Art Unit
	MICHAEL D BURKHART	1633

☑ Claims renumbered in the same order as presented by applicant ☐ CPA ☑ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	30	
/MICHAEL D BURKHART/ Primary Examiner, Art Unit 1633	15 July 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	none

U.S. Patent and Trademark Office — Part of Paper No.: 20230715

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	18/066,420	Russell et al.
	Examiner	Art Unit
	MICHAEL D BURKHART	1633

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name search (OC search, USPat, USPgPub, EPO, JPO, Derwent) keyword search (OC search, Google)	06/16/2023	MB
STIC search SEQ ID Nos	06/16/2023	MB
updated	07/15/2023	MB

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
none	none	07/15/2023	MB

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	18066420
Filing Date	2022-12-15
First Named Inventor	Ronnie M. Russell
Art Unit	1633
Examiner Name	BURKHART, MICHAEL D
Attorney Docket Number	INH-014US

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080227736	A1	2008-09-18	Chen et al.	
	1	20200371088	A1	2020-11-26	Birnbaum et al.	
	1	20210106632	A1	2021-04-15	KIM et al.	
	1	20190055568	A1	2019-09-18	Chen et al.	
	1	20200371088	A1	2020-11-26	FUSIL et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.D.B/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99**)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	1633
	Examiner Name	BURKHART, MICHAEL D
	Attorney Docket Number	INH-014US

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2020223240	WO	A1	2020-11-05	The Broad Institute, Inc		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	International Search Report and Written Opinion for PCT/US2022/081616, dated June 15, 2023, 14 pages.	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/MICHAEL D BURKHART/	Date Considered	07/15/2023

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	18066420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	1633
	Examiner Name	BURKHART, MICHAEL D
	Attorney Docket Number	INH-014US

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☒ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Christopher R. Bodle/	Date (YYYY-MM-DD)	2023-06-28
Name/Print	Christopher R. Bodle	Registration Number	80,876

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Bibliographic Data

Application No: 18/066,420

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged: /MICHAEL D BURKHART/ (Examiner's Signature) /MB/ (Initials)

Title: PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
12/15/2022	424	1633	INH-014US
RULE			

APPLICANTS

INTERIUS BIOTHERAPEUTICS, INC., Philadelphia, PA, UNITED STATES

INVENTORS

Ronnie M. Russell, Philadelphia, PA, UNITED STATES

Philip R. Johnson, Philadelphia, PA, UNITED STATES

James I. Andorko, Philadelphia, PA, UNITED STATES

Mohit Sachdeva, Philadelphia, PA, UNITED STATES

Bruce Schnepp, Havertown, PA, UNITED STATES

Michael Marinelli, Philadelphia, PA, UNITED STATES

Jeffrey Foss, Philadelphia, PA, UNITED STATES

Debasish Boral, Philadelphia, PA, UNITED STATES

CONTINUING DATA

This application has PRO of 63267039 01/21/2022

This application has PRO of 63266044 12/27/2021

This application has PRO of 63289977 12/15/2021

This application has PRO of 63289888 12/15/2021

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

03/23/2023

** SMALL ENTITY **

STATE OR COUNTRY

UNITED STATES

ADDRESS

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210
UNITED STATES

FILING FEE RECEIVED

$3,600

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L19	51	ronnie near2 russell.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:20 PM
L20	608	philip near2 johnson.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:20 PM
L21	6	james near2 andorko.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:20 PM
L22	1	mohit near2 sachdeva.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:20 PM
L23	11	bruce near2 schnepp.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L24	31	michael near2 marinelli.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L25	6	jeffrey near2 foss.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L26	0	debasish near2 boral.in.	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L27	26036649	(vsvg OR vsv-g OR (vesicular ADJ stomatitis ADJ virus)) NEAR 5 (envelope OR SU OR surface)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L28	0	L10 WITH (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L29	0	L10 SAME (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L30	640	L10 AND (i182$1 OR l198$1)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L31	14	L10 AND (i182e OR l198e)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L32	28	L10 AND (i182a OR l198a)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM
L33	345	L10 AND (i182 OR l198)	(US-PGPUB; USPAT; EPO; DERWENT)	OR	OR	OR	2023/07/15 07:21 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**08/01/2023 04:32:36 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Christopher Bodle
PATENT CENTER #	62539055	FILING DATE	12/15/2022
CUSTOMER #	51414	FIRST NAMED INVENTOR	Ronnie M. Russell
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Christopher Bodle

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
CorrectedADS.pdf	5	Application Data Sheet to update/correct info	106 KB
INH-014US_aia0040-as-filed.pdf	3	Request under Rule 48 correcting inventorship	235 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
CorrectedADS.pdf	6EB77E80DDC7CF842C11FDE347727356E9B53B44183540E81 695D82BDCD53E61D9CB78AC4DB8BAAC9258B0234BE8E6913

853C90DAC1234D8932F3AE064C1A7AA

INH-014US_aia0040-as-filed.pdf	3C31AB175796374D9D2376F97745E76C0A17C001EBB361D123 489450FEF82F99D8FE0CFDA9445BB2CB0486B9927E5D62B19 AB1A72A114E099092C0A06DB0404F

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**08/01/2023 04:32:36 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Christopher Bodle
PATENT CENTER #	62539055	AUTHORIZED BY	Christopher Bodle
CUSTOMER #	51414	FILING DATE	12/15/2022
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Ronnie M. Russell

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 1146	E202381G34567718	Julianne Holland

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2830	PROCESSING FEE, EXCEPT IN PROVISIONAL APPLICATIONS	56.00	1	56.00
			TOTAL AMOUNT:	**$56.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

Corrected Application Data Sheet

18066420 : PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

~~Strike-through~~ indicates removal of data from existing record Underline indicates new data being added to the application If no data is shown, no data has been corrected

Inventor Information

Data of record	Updated Data

Ronnie M. Russell

Residence Information
US Residency
Philadelphia, PA
UNITED STATES

Mailing Address
3401 Grays Ferry Avenue
Building 200, Suite 300
Philadelphia, PA 19146
UNITED STATES

Philip R. Johnson

Residence Information
US Residency
Philadelphia, PA
UNITED STATES

Mailing Address
3401 Grays Ferry Avenue
Building 200, Suite 300
Philadelphia, PA 19146
UNITED STATES

~~James I. Anderke~~

Residence Information
~~US Residency~~
~~Philadelphia, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

~~Mohit Sachdeva~~

Residence Information
~~US Residency~~
~~Philadelphia, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

~~Bruce Schnepp~~

Residence Information
~~US Residency~~
~~Havertown, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

~~Michael Marinelli~~

Residence Information
~~US Residency~~
~~Philadelphia, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

~~Jeffrey Foss~~

Residence Information
~~US Residency~~
~~Philadelphia, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

~~Debasish Boral~~

Residence Information
~~US Residency~~
~~Philadelphia, PA~~
~~UNITED STATES~~

Mailing Address
~~3401 Grays Ferry Avenue~~
~~Building 200, Suite 300~~
~~Philadelphia, PA 19146~~
~~UNITED STATES~~

Application Information

Title of Invention	PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF
Attorney Docket Number	INH-014US
Entity Status	Small

Domestic Benefit/National Stage Information

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c), 386(c), or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.

Data of record	Updated Data

No data change in this section

Foreign Priority Information

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the Application Data Sheet constitutes the claim for priority as required by 35 U.S.C. 119 (b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX) the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Data of record	Updated Data

No data change in this section

Applicant Information

The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46.

Data of record	Updated Data

No data change in this section

Assignee Information including Non-Applicant Assignee Information

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Data of record	Updated Data

No data change in this section

Signature

NOTE:

This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See CFR 1.4(d) for the manner of making signatures and certifications.

Signature	First name	Last name	Registration #	Date
/Christopher Bodle/	Christopher	Bodle	80876	08/01/2023

Doc Code: R48.REQ
Document Description: Request under Rule 48 correcting inventorship

PTO/AIA/40 (04-18)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR CORRECTION IN A PATENT APPLICATION RELATING TO INVENTORSHIP OR AN INVENTOR NAME, OR ORDER OF NAMES, OTHER THAN IN A REISSUE APPLICATION (37 CFR 1.48)		
	Application Number	18/066,420
	Filing Date	2022-12-15
	First Named Inventor	Ronnie M. Russell
	Art Unit	1633
	Examiner Name	MICHAEL D BURKHART
	Practitioner Docket Number	INH-014US

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Applicant hereby **requests that the inventorship be corrected or changed, or that the name of the inventor or a joint inventor, or the order of the names of joint inventors, be changed,** in the above-identified application. **Note**: 37 CFR 1.48 applies to any request to correct inventorship filed on or after September 16, 2012, regardless of the application filing date. **Do not submit this form after payment of the issue fee or if the application has been patented.** See 37 CFR 1.324 for correction of inventorship in a patent.

Please check the applicable box(es) below.

For a nonprovisional application:

☒ 1. This request is to correct or change the inventorship in a **nonprovisional** application (**under 37 CFR 1.48(a)**) and includes:

☒ An application data sheet (ADS) in accordance with 37 CFR 1.76(c) with the corrected or updated information shown with markings (*e.g.*, underlining for insertions, strikethrough for deletions). See the Manual of Patent Examining Procedure (MPEP) section 601.05(a) for information about filing an ADS in an application filed on/after September 16, 2012. For information about filing a Supplemental ADS in an application filed before September 16, 2012, see MPEP 601.05(b).

☒ The processing fee set forth in 37 CFR 1.17(i). $ 56.00

☐ An inventor is being added. An inventor's oath or declaration by any actual inventor who has not yet executed an oath or declaration is required (see 37 CFR 1.48(b)). See MPEP 602.01(a) for information about an inventor's oath or declaration for an application filed on/after September 16, 2012 (*e.g.*, form **PTO/AIA/01**). For information about an inventor's oath or declaration for an application filed before September 16, 2012 (*e.g.*, form **PTO/SB/01**), see MPEP 602.01(b).

☒ This request is being filed after the first Office action on the merits has been given or mailed (see 37 CFR 1.48(c) and 1.17(d)). Check one of the following:

☒ This request to correct or change the inventorship is due solely to the cancellation of claims in the application.

OR

☐ The fee set forth in 37 CFR 1.17(d) is due (in addition to the fee set forth in 37 CFR 1.17(i)). $ _____

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0031. Public burden for this form is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **If filing this completed form by mail, send to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/AIA/40 (04-18)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR CORRECTION IN A PATENT APPLICATION RELATING TO INVENTORSHIP OR AN INVENTOR NAME, OR ORDER OF NAMES, OTHER THAN IN A REISSUE APPLICATION (37 CFR 1.48)

☐ 2. This request is to correct or update the name of the inventor or a joint inventor, or the order of names of joint inventors, in a **nonprovisional** application (**under 37 CFR 1.48(f)**) and includes:

☐ An application data sheet in accordance with 37 CFR 1.76(c) identifying the complete inventive entity, including the corrected or updated name of the inventor, or the new order of names shown with markings (*e.g.*, underlining for insertions, strikethrough for deletions). See the MPEP 601.05(a) for information about filing an ADS in an application filed on/after September 16, 2012. For information about filing a Supplemental ADS in an application filed before September 16, 2012, see MPEP 601.05(b).

☐ The processing fee set forth in 37 CFR 1.17(i). $ _____

For a provisional application:

☐ This request is to change or correct the inventorship, or correct or update the name of the inventor or a joint inventor, in a **provisional** application (**under 37 CFR 1.48(d)**) and includes:

☐ **Attached hereto** is a document that is signed by a party set forth in 37 CFR 1.33(b) and identifies each inventor by his or her legal name, in the preferred order. Note: the document may be an application data sheet in accordance with 37 CFR 1.76(c) that identifies the changes with markings (underlining for insertions, strikethrough for deletions).

☐ The processing fee set forth in 37 CFR 1.17(q). $ _____

Fee Payment Information:

■ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

■ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 07-1700.

■ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ Applicant*

■ attorney or agent of record
Registration number 80,876

☐ attorney or agent acting under 37 CFR 1.34
Registration number _____

Signature /Christopher R. Bodle/

Typed or printed name Christopher R. Bodle

Date 2023-08-01

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. *Juristic entities must be represented by a patent practitioner (See 37 CFR 1.31, applicable to any paper filed on or after September 16, 2012 that is presented on behalf of a juristic entity, regardless of application filing date). Submit multiple forms if more than one signature is required, see below**.

☐ ** Total of _____ forms are submitted.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013). https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to: 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law; 2) a Federal, state, local, or international agency, in response to its request; 3) a contractor of the USPTO having need for the information in order to perform a contract; 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record; 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record; 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations; 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals; 8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)); 9) the Office of Personnel Management (OPM) for personnel research purposes; and 9) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Additional Uses

Additional USPTO uses of the information in this record may include disclosure to: 1) the International Bureau of the World Intellectual Property Organization, if the record is related to an international application filed under the Patent Cooperation Treaty; 2) the public i) after publication of the application pursuant to 35 U.S.C. 122(b), ii) after issuance of a patent pursuant to 35 U.S.C. 151, iii) if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections, or an issued patent, or iv) without publication of the application or patent under the specific circumstances provided for by 37 CFR 1.14(a)(1)(v)-(vii); and/or 3) the National Archives and Records Administration, for inspection of records.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
18/066,420	12/15/2022	1633	1760	INH-014US	23	1

CONFIRMATION NO. 1909

UPDATED FILING RECEIPT

51414
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

Date Mailed: 08/04/2023

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Ronnie M. Russell, Philadelphia, PA;
Philip R. Johnson, Philadelphia, PA;

Applicant(s)

INTERIUS BIOTHERAPEUTICS, INC., Philadelphia, PA;

Power of Attorney: The patent practitioners associated with Customer Number 051414

Domestic Priority data as claimed by applicant

This appln claims benefit of 63/289,888 12/15/2021
and claims benefit of 63/289,977 12/15/2021
and claims benefit of 63/266,044 12/27/2021
and claims benefit of 63/267,039 01/21/2022

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 03/23/2023
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/066,420**
Projected Publication Date: 08/17/2023
Non-Publication Request: No
Early Publication Request: No
**** SMALL ENTITY ****
Title

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Preliminary Class

424

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US

CONFIRMATION NO. 1909

51414
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

37 CFR 1.48 ACKNOWLEDGEMENT LETTER

OC000000060141422

Date Mailed: 08/04/2023

NOTICE OF ACCEPTANCE OF REQUEST UNDER 37 CFR 1.48(a)

This is in response to the applicant's request under 37 CFR 1.48(a) submitted on 08/01/2023.

The request under 37 CFR 1.48(a) to correct the inventorship, to correct or update the name of an inventor, or to correct the order of names of joint inventors is accepted.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/ttran/

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**08/04/2023 02:03:06 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Julianne Holland
PATENT CENTER #	62562156	AUTHORIZED BY	Christopher Bodle
CUSTOMER #	51414	FILING DATE	12/15/2022
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Ronnie M. Russell

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 1146	E202384E04386410	Christopher Bodle

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2501	UTILITY ISSUE FEE	480.00	1	480.00
			TOTAL AMOUNT:	**$480.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ISSUE FEE TRANSMITTAL FORM

APPLICATION #	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET #
18066420	12/15/2022	Ronnie Russell	INH-014US

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Nonprovisional Application under 35 USC 111(a)	DATE DUE	10/26/2023
CONFIRMATION #	1909	ISSUE FEE DUE	$ 480
EXAMINER	MICHAEL BURKHART	PUBLICATION DUE	$ 0
GROUP ART UNIT	1633	TOTAL FEES DUE	$480
CLASS - SUBCLASS	424/130100	PREV. PAID FEE	$ 0
ENTITY STATUS	Small		

1. CHANGE OF CORRESPONDENCE ADDRESS AND/OR INDICATION OF FEE ADDRESS (37 CFR 1.33 & 1.363)

Correspondence Address

CURRENT ADDRESS

Maintenance Fee Address

CURRENT ADDRESS

☐ Change of correspondence address requested,system generated AIA/122-PC form attached

☐ Fee address indication requested, system generatedSB/47-PC form attached

2. ENTITY STATUS

Change in Entity Status

NEW STATUS

3. THE FOLLOWING FEES ARE SUBMITTED

☑ Issue Fee

☑ Publication Fee

4. FEE AUTHORIZATION

☐ I authorize USPTO to apply my previously paid issue fee to the current fees due

☐ The Director is herby authorized to apply my previously paid issue fee to the current fee due and to charge deficient fees to Deposit Account Number:

☑ If in addition to the payment of the issue fee amount submitted with this form, there are any discrepencies in any amount(s) due, the Director is authorized to charge any deficiency, or credit any overpayment, to Deposit Account Number: 71700

5. FIRM AND/OR ATTORNEY NAMES TO BE PRINTED

NOTE: If no name is listed, no name will be printed
For printing on the patent front page, list to be displayed as entered

Goodwin Procter LLP

6. ASSIGNEE NAME(S) AND RESIDENCE DATA TO BE PRINTED

NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

INTERIUS BIOTHERAPEUTICS, INC. Philadelphia , PA UNITED STATES Corporation

Signature

I certify, in accordance with 37 CFR 1.4(d)(4) that I am an attorney or agent registered to practice before the

Patent and Trademark Office who has filed and has been granted power of attorney in this application. I also certify that this Fee(s) Transmittal form is being transmitted to the USPTO via Patent Center on the date indicated below.

Signature	Name	Registration #	Date
/Christopher Bodle/	Christopher Bodle	80876	08/04/2023

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/066,420	**08/04/2023 02:03:06 PM ET**	**INH-014US**

Title of Invention

PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	1909	FILED BY	Julianne Holland
PATENT CENTER #	62562156	FILING DATE	12/15/2022
CUSTOMER #	51414	FIRST NAMED INVENTOR	Ronnie M. Russell
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Christopher Bodle

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
web85b.pdf	3	Issue Fee Payment (PTO-85B)	61 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
web85b.pdf	F34A8A1FB31AC1B5FEAA9FBA6708ED41601B16696AF55D562 27CEB84DDBC6881554C67DA1C38DBD56A6D60F3EF37AB640 6EE44E52A77371EB0A1172680D06F53

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized

by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	09/26/2023	11767366	INH-014US	1909

51414 7590 09/06/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at https://certifiedcopycenter.uspto.gov/index.html. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (https://patentcenter.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

Ronnie M. Russell, Philadelphia, PA;
Philip R. Johnson, Philadelphia, PA;

APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

INTERIUS BIOTHERAPEUTICS, INC., Philadelphia, PA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US

CONFIRMATION NO. 1909

51414
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

PUBLICATION NOTICE

OC000000062228759

Date Mailed: 09/22/2023

Title:PSEUDOTYPED VIRAL PARTICLES, COMPOSITIONS COMPRISING THE SAME, AND USES THEREOF

Publication No.US-2023-0295332-A1
Publication Date:09/21/2023

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/066,420	12/15/2022	Ronnie M. Russell	INH-014US	1909

51414 7590 09/26/2023

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/26/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

JGoodwin@goodwinlaw.com
PSousa-Atwood@goodwinlaw.com
US-PatentBos@goodwinlaw.com

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.
18/066,420	26-Sep-2023	11767366

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
100 NORTHERN AVENUE
BOSTON, MA 02210

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at https://patentcenter.uspto.gov

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit https://www.uspto.gov/electronicgrants