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UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

December 28, 2022

**THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
RECORDS OF THIS OFFICE OF THE FILE WRAPPER AND CONTENTS
OF:**

APPLICATION NUMBER: 14/006,641

FILING DATE: May 05, 2014

PATENT NUMBER: 9987308

ISSUE DATE: June 05, 2018



Certified by

Kathi

Performing the Functions and Duties of the
Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	ATTY. DOCKET NO. 360056.420USPC	APPLICATION NO. 14/006,641
	APPLICANTS Stanley R. Riddell <i>et al.</i>	
	INTERNATIONAL FILING DATE March 23, 2012	GROUP ART UNIT

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	KIND CODE	DATE	NAME	FILING DATE IF APPROPRIATE
	1	4,690,915		09/01/87	Rosenberg	
	2	6,040,177	A	03/21/00	Riddell et al.	
	3	2003/0170238	A1	09/11/03	Gruenberg et al.	
	4	2008/0131415	A1	06/05/08	Riddell et al.	
	5					

FOREIGN PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	KIND CODE	DATE	COUNTRY	TRANSLATION YES NO
	1	WO 2010/025177	A1	03/04/10	WO	
	2					
	3					
	4					

NON-PATENT LITERATURE DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

	1	BASKAR et al., "Unique Cell Surface Expression of Receptor Tyrosine Kinase ROR1 in Human B-Cell Chronic Lymphocytic Leukemia," <i>Clin. Cancer Res.</i> 14(2): 396-404, January 15, 2008
	2	BERGER et al., "Adoptive transfer of effector CD8+ T cells derived from central memory cells establishes persistent T cell memory in primates," <i>The Journal of Clinical Investigation</i> 118(1): 294-305, January 2008
	3	BERGER et al., "Adoptive transfer of virus-specific and tumor-specific T cell immunity," <i>Current Opinion in Immunology</i> 21: 224-232, 2009
	4	BLATTMAN et al., "Cancer Immunotherapy: A Treatment for the Masses," <i>Science</i> 305: 200-205, July 9, 2004
	5	BLEAKLEY et al., "Molecules and mechanisms of the graft-versus-leukaemia effect," <i>Nature Reviews Cancer</i> 4: 371-380, May 2004
	6	BOLLARD et al., "Cytotoxic T Lymphocyte Therapy for Epstein-Barr Virus ⁺ Hodgkin's Disease," <i>J. Exp. Med.</i> 200(12): 1623-1633, December 20, 2004
	7	BRENTJENS et al., "Eradication of systemic B-cell tumors by genetically targeted human T lymphocytes co-stimulated by CD80 and interleukin-15," <i>Nature Medicine</i> 9(3): 279-286, March 2003
	8	BUTCHER et al., "Lymphocyte homing and homeostasis," <i>Science</i> 272(5258): 60, 1996, 13 pages

EXAMINER	DATE CONSIDERED
* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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9	CHEADLE et al., "Natural Expression of the CD19 Antigen Impacts the Long-Term Engraftment but Not Antitumor Activity of CD19-Specific Engineered T Cells," <i>The Journal of Immunology</i> 184(4): 1885-1896, January 20, 2010
10	CHEEVER et al., "Specificity of adoptive chemoimmunotherapy of established syngeneic tumors," <i>The Journal of Immunology</i> 125(2): 711-714, August 1980
11	DUDLEY et al., "Adoptive Transfer of Cloned Melanoma-Reactive T Lymphocytes for the Treatment of Patients with Metastatic Melanoma," <i>Journal of Immunotherapy</i> 24(4): 363-373, 2001
12	DUDLEY et al., "A phase I Study of Nonmyeloablative Chemotherapy and Adoptive Transfer of Autologous Tumor Antigen-Specific T Lymphocytes in Patients With Metastatic Melanoma," <i>J. Immunother.</i> 25(3): 243-251, 2002
13	DUDLEY <i>et al.</i> , "Cancer Regression and Autoimmunity in Patients After Clonal Repopulation with Antitumor Lymphocytes," <i>Science</i> 298(5594): 850-854, October 25, 2002
14	DUDLEY et al., "Adoptive Cell Transfer Therapy Following Non-Myeloablative but Lymphodepleting Chemotherapy for the Treatment of Patients With Refractory Metastatic Melanoma," <i>J. Clin. Oncol.</i> 23(10): 2346-2357, April 1, 2005
15	FUKUDA et al., "Antisera induced by infusions of autologous Ad-CD154-leukemia B cells identify ROR1 as an oncofetal antigen and receptor for Wnt5a," <i>Proc. Natl. Acad. Sci. U S A</i> 105(8): 3047-3052, February 26, 2008
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17	GATTINONI et al., "Adoptive immunotherapy for cancer: building on success," <i>Nat. Rev. Immunol.</i> 6(5): 383-393, May 2006
18	HUDECEK et al., "Naïve CD4+ T Cells Modified to Express a ROR1-Specific CAR Mediate Anti-Tumor Activity and Provide Superior Help to CD8+ ROR1-CAR T Cells," <i>Blood</i> (ASH Annual Meeting Abstracts) 118: Abstract 643, 2011, 3 pages
19	KESSELS et al., "Immunotherapy through TCR gene transfer," <i>Nature Immunology</i> 2(10): 957-961, October 2001
20	KLEIN et al., "Gene Expression Profiling of B Cell Chronic Lymphocytic Leukemia Reveals a Homogeneous Phenotype Related to Memory B Cells," <i>J. Exp. Med.</i> 194(11): 1625-1638, December 3, 2001
21	LAPALOMBELLA et al., "Lenalidomide treatment promotes CD154 expression on CLL cells and enhances production of antibodies by normal B cells through a PI3-kinase-dependent pathway," <i>Blood</i> 115(13): 2619-2629, April 1, 2010
22	MITSUYASU et al., "Prolonged survival and tissue trafficking following adoptive transfer of CD4ζ gene-modified autologous CD4+ and CD8+ T cells in human immunodeficiency virus-infected subjects," <i>Blood</i> 96(3): 785-793, August 2000

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23	MORGAN et al., "Cancer Regression in Patients After Transfer of Genetically Engineered Lymphocytes," <i>Science</i> 314(5796): 126-129, October 6, 2006
24	PAHL-SEIBERT et al., "Highly Protective In Vivo Function of Cytomegalovirus IE1 Epitope-Specific Memory CD8 T Cells Purified by T-Cell Receptor-Based Cell Sorting," <i>Journal of Virology</i> 79(9): 5400-5413, May 2005
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27	ROONEY et al., "Infusion of Cytotoxic T Cells for the Prevention and Treatment of Epstein-Barr Virus-Induced Lymphoma in Allogeneic Transplant Recipients," <i>Blood</i> 92(5): 1549-1555, September 1, 1998
28	ROSENWALD et al., "Relation of Gene Expression Phenotype to Immunoglobulin Mutation Genotype in B Cell Chronic Lymphocytic Leukemia," <i>The Journal of Experimental Medicine</i> 194(11): 1639-1647, December 3, 2001
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32	STANISLAWSKI et al., "Circumventing tolerance to a human MDM2-derived tumor antigen by TCR gene transfer," <i>Nature Immunology</i> 2(10): 962-970, October 2001
33	WALTER et al., "Reconstitution of cellular immunity against cytomegalovirus in recipients of allogeneic bone marrow by transfer of T-cell clones from the donor," <i>N. Engl. J. Med.</i> 333: 1038-1044, October 19, 1995
34	WANG et al., "Cellular Immunotherapy for Follicular Lymphoma Using Genetically Modified CD20-Specific CD8 ⁺ Cytotoxic T Lymphocytes," <i>Molecular Therapy</i> 9(4): 577-586, April 2004
35	YEE et al., "Adoptive T cell therapy using antigen-specific CD8 ⁺ T cell clones for the treatment of patients with metastatic melanoma: <i>In vivo</i> persistence, migration, and antitumor effect of transferred T cells," <i>Proc. Natl. Acad. Sci. USA</i> 99(25): 16168-16173, December 10, 2002

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PATENT COOPERATION TREATY

Applicants : Stanley R. Riddell *et al.*
Int'l Application No. : PCT/US2012/030388
U.S. Application No. : 14/006,641
Int'l Filing Date : March 23, 2012
Title : METHOD AND COMPOSITIONS FOR CELLULAR
IMMUNOTHERAPY

Docket No. : 360056.420USPC

Date : March 10, 2014

Mail Stop PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Commissioner for Patents:

In accordance with 37 CFR §§1.56 and 1.97 through 1.98, Applicants wish to make known to the U.S. Patent and Trademark Office the references set forth on the attached Information Disclosure Statement. Copies of cited U.S. patents and published patent applications are not required and accordingly have not been provided. Copies of any other cited references are enclosed. As to any reference cited, Applicants do not admit that it is “prior art” under 35 U.S.C. §§102 or 103, and specifically reserve the right to traverse or antedate any such reference, as by a showing under 37 CFR §1.131 or other method. Although the aforesaid references are made known to the Patent and Trademark Office in compliance with Applicants’ duty to disclose all information they are aware of that is believed relevant to the examination of the above-identified application, Applicants believe that their invention is patentable.

Please acknowledge receipt of this Information Disclosure Statement and kindly make the cited references of record in the above-identified application.

Applicants believe this Information Disclosure Statement has been timely filed, however, the Director is authorized to charge any fee due by way of this Information Disclosure Statement to our Deposit Account No. 19-1090.

Respectfully submitted,
SEED Intellectual Property Law Group PLLC

/Jeffrey C. Pepe/
Jeffrey C. Pepe, Ph.D.
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JCP:cw

Enclosures:
Information Disclosure Statement (3 pages)
Cited References (36)

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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	ATTY. DOCKET NO. 360056.420USPC	APPLICATION NO. 14/006,641
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FOREIGN PATENT DOCUMENTS

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	1	WO 2006/060878	A1	06/15/06	WO		
	2						

NON-PATENT LITERATURE DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

	1	ALTENSCHMIDT et al., "Cytolysis of Tumor Cells Expressing the Neu/erbB-2, erbB-3, and erbB-4 Receptors by Genetically Targeted Naive T Lymphocytes," <i>Clinical Cancer Research</i> 2: 1001-1008, June 1996
	2	ALTENSCHMIDT et al., "Adoptive Transfer of In Vitro-Targeted, Activated T Lymphocytes Results in Total Tumor Regression," <i>The Journal of Immunology</i> 159: 5509-5515, 1997
	3	HINRICHS et al., "Adoptively transferred effector cells derived from naïve rather than central memory CD8 ⁺ T cells mediate superior antitumor immunity," <i>PNAS</i> 106(41): 17469-17474, October 13, 2009
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	5	HUDECEK et al., "The B-cell tumor-associated antigen ROR1 can be targeted with T cells modified to express a ROR1-specific chimeric antigen receptor," <i>Blood</i> 116(22): 4532-4541, 2010
	6	KERSHAW et al., "Gene-Engineered T Cells as a Superior Adjuvant Therapy for Metastatic Cancer," <i>The Journal of Immunology</i> 173: 2143-2150, 2004
	7	MOELLER et al., "Adoptive transfer of gene-engineered CD4 ⁺ helper T cells induces potent primary and secondary tumor rejection," <i>Blood</i> 106: 2995-3003, 2005
	8	TENG et al., "Immunotherapy of Cancer Using Systemically Delivered Gene-Modified Human T Lymphocytes," <i>Human Gene Therapy</i> 15: 699-708, July 2004
	9	WALKER et al., "Long-term in vivo survival of receptor-modified syngeneic T cells in patients with human immunodeficiency virus infection," <i>Blood</i> 96: 467-474, 2000
	10	WANG et al., "Engraftment of human central memory-derived effector CD8 ⁺ T cells in immunodeficient mice," <i>Blood</i> 117(6): 1888-1898, 2011
	11	WESTWOOD et al., "Genetic redirection of T cells for cancer therapy," <i>Journal of Leukocyte Biology</i> 87: 791-803, May 2010

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Applicants : Stanley R. Riddell *et al.*
Int'l Application No. : PCT/US2012/030388
U.S. Application No. : 14/006,641
Int'l Filing Date : March 23, 2012
Title : METHOD AND COMPOSITIONS FOR CELLULAR
IMMUNOTHERAPY

Docket No. : 360056.420USPC

Date : May 12, 2014

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/006,641	05/05/2014	Stanley R. Riddell	360056.420USPC	5681

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EXAMINER

BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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05/04/2016

PAPER

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.

Office Action Summary	Application No. 14/006,641	Applicant(s) RIDDELL ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	AIA (First Inventor to File) Status No

-- 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 21 April 2016; 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) 39-70 is/are pending in the application.
5a) Of the above claim(s) 43,48,57 and 68 is/are withdrawn from consideration.
- 6) ☐ Claim(s) _____ is/are allowed.
- 7) ☒ Claim(s) 39-42,44-47,49,51-56,58-61,63-67,69 and 70 is/are rejected.
- 8) ☒ Claim(s) 50 and 62 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 3/10/14;5/12/14;2/8/16;3/11/16.
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 4) ☐ Other: _____.

Miltenyi Ex. 1008 Page 11

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Election/Restrictions

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (“requirement of unity of invention”). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression “special technical features” shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

Art Unit: 1633

WHEN CLAIMS ARE DIRECTED TO MULTIPLE CATEGORIES OF INVENTIONS

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Species I, elect one specific antigen, e.g. as recited in claims 40-43, 54-57, 66-68;

Species II, elect either “same” or “different” intracellular signaling domains, e.g. as recited in claims 47-48

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify

Art Unit: 1633

the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise require all the limitations of an allowed generic claim. Currently, the following claim(s) are generic: claim 39

The groups of inventions listed above 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 species are mutually exclusive and thus cannot share a special technical feature.

During a telephone conversation with Jeff Pepe on 4/21/2016 a provisional election was made without traverse to prosecute the species of CD19 as antigen (claim 42) and the species of the same signaling domain (claim 47). Affirmation of this election must be made by applicant in replying to this Office action. Claims 43, 48, 57, 68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be corrected in compliance with 37 CFR 1.48(a) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. A request to correct inventorship under 37 CFR 1.48(a) must be accompanied by an

Art Unit: 1633

application data sheet in accordance with 37 CFR 1.76 that identifies each inventor by his or her legal name and by the processing fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39-42, 44-47, 49, 51-56, 58-61, 63-67, 69 and 70 are rejected under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Huang et al (2008, cited by applicants) in view of Berger et al (2009, cited by applicants) and Sallusto et al (cited by applicants).

Huang et al teach a T cell composition comprising CD4+ and CD8+ cells expressing a CD19-specific chimeric antigen receptor (CAR) that in turn comprises a CD19 scFv, a transmembrane domain, a 4-1BB signaling domain and a CD3 intracellular domain. See, e.g. the abstract and Fig. 1a. Thus, both T cell subsets are considered to have the same intracellular signaling domain. The T cells used are considered autologous relative to the organism from which they were derived. The CAR T cells were used in methods of immunotherapy of CD19+ tumor cells (e.g., page 585). The CD4+ cells expressed CD62L (page 585, second col.), considered to be CD62L+ as recited in the claims absent a definitive definition, and were 95% of the population. Huang et al do not specifically teach that the CD8+ cells were CD62L+ and CD45RO+, nor that the CD4+ cells were CD45RA+, CD45RO- CD62L+ naive cells. However,

Art Unit: 1633

Berger et al teaches that the pool of T cells for immunotherapy inherently comprises naive CD45RA+ CD62L+ cells and CD45RO+ CD62L+ central memory cells (page 227, second col., first ¶). Likewise, Sallusto et al teach (e.g. Figure 1) that CD8+ memory cells are CD62L+ CD45RO+.

Allowable Subject Matter

Claims 50 and 62 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. There are no teachings in the prior art of compositions comprising both CD4+ naive and CD4+ central memory cells as recited in claims 50 and 62.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

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 an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Stanley R. Riddell *et al.*
Application No. : 14/006,641
Filed : May 5, 2014
For : METHOD AND COMPOSITIONS FOR CELLULAR
IMMUNOTHERAPY

Examiner : Michael D. Burkhart
Art Unit : 1633
Docket No. : 360056.420USPC
Date : October 4, 2016

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY AND AMENDMENT UNDER 37 C.F.R. §§1.111 AND 1.121

Commissioner for Patents:

Further to the Office Action dated May 4, 2016, please extend the time for response two (2) months, to expire on October 4, 2016. Enclosed is a Petition for an Extension of Time, along with the requisite fee. Please enter into the record of the above-identified application the following:

Amendments to the Claims, which are reflected in the Listing of Claims and begin on page 2 of this paper; and

Remarks, which begin on page 13 of this paper.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Amendments to the Claims

Please cancel claims 41, 46, 51, 52, 55, 60, and 62-64 without prejudice; amend claims 39, 40, 42-45, 47-50, 53, 54, 56-59, 61, and 65-70; and add new claims 71-85, as shown below. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. – 38. (Canceled)

39. (Currently Amended) An adoptive cellular immunotherapy composition ~~consisting essentially of comprising~~ chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein:

(a) ~~the chimeric antigen receptor-modified CD4⁺ T lymphocytes in the composition consist of a-helper T lymphocytes cell preparation of CD62L⁺ CD4⁺ cells genetically modified to express an antigen-reactive that contain a~~ chimeric antigen receptor ~~that specifically binds to an antigen, and~~

(b) ~~the chimeric antigen receptor-modified CD8⁺ T lymphocytes in the composition consist of CD8⁺ a-cytotoxic T lymphocytes cell preparation of CD45RO⁺ CD62L⁺ CD8⁺ that are derived from a central memory-enriched CD8⁺ cells genetically modified to express an antigen-reactive population and contain a~~ chimeric antigen receptor ~~that specifically binds to the antigen;~~

~~wherein the genetically modified CD4⁺ T helper cells are capable of eliciting direct antigen recognition and augmenting the CD8⁺ cellular immune response.~~

40. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein the antigen is associated with a disease or disorder selected from a solid tumor, hematologic malignancy, melanoma, ~~or viral and infection with a pathogen.~~

41. (Canceled)

42. (Currently Amended) The adoptive cellular immunotherapy composition according to claims 39, wherein the antigen is ~~an orphan tyrosine kinase receptor selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA, or hepatitis B surface antigen.~~

43. (Withdrawn – Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein the antigen is a pathogen specific cell surface antigen selected from an HIV antigen, an HCV antigen, an HBV antigen, a hepatitis B surface antigen, a CMV antigen, ~~or and~~ a parasitic antigen.

44. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody fragment specific for an antigen associated with a disease or disorder, and an intracellular signaling module.

45. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 44, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4+ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8+ T lymphocytes, individually, comprises a transmembrane domain, (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB-signaling costimulatory domain, and a CD3 intracellular signaling domain.

46. (Canceled)

47. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein (a) the intracellular signaling domain of the chimeric antigen receptor is contained by the CD8+ cytotoxic T-cells lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor is contained by the CD4+ helper T-cells

lymphocytes, or (b) the chimeric antigen receptor contained by the CD8+ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4+ T lymphocytes.

48. (Withdrawn – Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein (a) the intracellular signaling domain of the chimeric antigen receptor in the CD8+ cytotoxic T-cells lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4+ helper T-cells lymphocytes; or (b) the chimeric antigen receptor contained by the CD8+ T lymphocytes is different than the chimeric antigen receptor contained by the CD4+ T lymphocytes.

49. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein the genetically (a) at least 60% of the chimeric antigen receptor-modified helper CD4+ T lymphocytes cell preparation contains at least 80% are surface positive for CD62L and CD45RA or CD45RO+ CD4+ helper T-cells; or (b) at least 80% of the chimeric antigen receptor-modified CD4+ T lymphocytes are surface positive for CD62L and CD45RA or CD45RO.

50. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 39, wherein the CD4+ helper T lymphocytes cell preparation consists essentially of are derived from (a) a CD45RA+ CD45RO- CD62L+ CD4+ naïve T cells-enriched CD4+ population; (b) and CD45RA- CD45RO+ CD62L+ CD4+ central memory T cells-enriched CD4+ population; (c) a CD45RA+ CD62L+ naïve T cell-enriched and CD45RO+ CD62L+ central memory T cell-enriched CD4+ population; or (d) a bulk CD4+ T cell population genetically modified to express an antigen-reactive chimeric antigen receptor.

51., 52. (Canceled)

53. (Currently Amended) An adoptive cellular immunotherapy composition ~~comprising~~ containing chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein:

(a) ~~a helper~~ the chimeric antigen receptor-modified CD4⁺ T lymphocytes ~~cell preparation consisting essentially of CD62L⁺ CD4⁺ cells genetically modified to express an antigen-reactive~~ contain a chimeric antigen receptor that specifically binds to an antigen and at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or CD45RA, and

(b) ~~an autologous antigen-specific cytotoxic~~ the chimeric antigen receptor-modified CD8⁺ T lymphocytes ~~cell preparation consisting essentially of CD45RO⁺ CD62L⁺ CD8⁺ central-memory cells;~~ contain a chimeric antigen receptor that specifically binds to the antigen and at least 50% of CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L and/or CD45RO

~~wherein the genetically modified CD4⁺ T helper cells are capable of eliciting direct antigen recognition and augmenting the CD8⁺ cellular immune response.~~

54. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is associated with a disease or disorder selected from a solid tumor, hematologic malignancy, melanoma, ~~or viral~~ and infection ~~with a pathogen~~.

55. (Canceled)

56. (Currently Amended) The adoptive cellular immunotherapy composition according to claims 53, wherein the antigen is ~~an orphan tyrosine kinase receptor~~ selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA, ~~or hepatitis B surface antigen~~.

57. (Withdrawn – Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is a pathogen specific cell surface

antigen selected from an HIV antigen, an HCV antigen, an HBV antigen, a hepatitis B surface antigen, a CMV antigen, ~~or~~ and a parasitic antigen.

58. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody fragment specific for an antigen associated with a disease or disorder, and an intracellular signaling module.

59. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 58, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes, individually, comprises a transmembrane domain; (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB-signaling costimulatory domain; and a CD3 intracellular signaling domain.

60. (Canceled)

61. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein ~~the genetically~~:

(a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA;

(b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO;

(c) at least 80% of the chimeric antigen receptor-modified-helper CD4⁺ T lymphocytes ~~cell preparation contains at least 80%~~ are surface positive for CD62L+CD4⁺ helper T-cells and/or CD45RA; and/or

(d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.

62. – 64. (Canceled)

65. (Currently Amended) A method of performing cellular immunotherapy in a ~~subject having a disease or disorder treating cancer, comprising administering a~~ subject having cancer the composition of claim 39.

66. (Currently Amended) The method according to claim 65, wherein the ~~antigen is a tumor associated cell surface antigen the cancer is selected from a solid tumor, hematologic malignancy, and melanoma.~~

67. (Currently Amended) The method according to claim ~~66~~ 65, wherein the antigen is ~~an orphan tyrosine kinase receptor selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA, or hepatitis B surface antigen.~~

68. (Withdrawn – Currently Amended) The method according to claim ~~65~~ 74, wherein the antigen is a pathogen specific cell surface antigen selected from an HIV antigen, an HCV antigen, an HBV antigen, a hepatitis B surface antigen, a CMV antigen, or and a parasitic antigen.

69. (Currently Amended) The method according to claim 65, wherein ~~the genetically:~~
(a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA;

(b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO;

(c) at least 80% of the chimeric antigen receptor-modified-helper CD4⁺ T lymphocytes cell preparation contains at least 80% are surface positive for CD62L+CD4⁺ helper T cells and/or CD45RA; and/or

(d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.

70. (Currently Amended) The method according to claim ~~69~~ 65, wherein the ~~at least 80% CD62L+~~ CD4+ helper T-cells lymphocytes are derived from (a) ~~CD45RA+ CD45RO- CD62L+ CD4+~~ naïve-helper T cells-enriched CD4+ population; (b) a CD45RO+ CD62L+ central memory T cell-enriched CD4+ population; (c) a CD45RA+ CD62L+ naïve T cell-enriched and CD45RO+ CD62L+ central memory T cell-enriched CD4+ population; or (d) a bulk CD4+ T cell population.

71. (New) The method according to claim 65, wherein the chimeric antigen receptor comprises an extracellular antibody variable domain or single-chain antibody fragment specific for an antigen associated with a disease or disorder, and an intracellular signaling module.

72. (New) The method according to claim 71, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4+ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8+ T lymphocytes, individually, comprise (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB costimulatory domain and a CD3 intracellular signaling domain.

73. (New) The method according to claim 65, wherein:

(a) the intracellular signaling domain of the chimeric antigen receptor contained by the CD8+ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4+ T lymphocytes;

(b) the chimeric antigen receptor contained by the CD8+ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4+ T lymphocytes;

(c) the intracellular signaling domain of the chimeric antigen receptor in the CD8+ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4+ T lymphocytes; or

(d) the chimeric antigen receptor contained by the CD8+ T lymphocytes is different than the chimeric antigen receptor contained by the CD4+ T lymphocytes.

74. (New) A method of treating an infectious disease, the method comprising administering to a subject having an infectious disease the composition of claim 39.

75. (New) The method according to claim 74, wherein the infectious disease is a viral infection.

76. (New) The method according to claim 75, wherein the viral infection is selected from an infection with a herpes virus, a retrovirus, and a flavivirus.

77. (New) The method according to claim 76, wherein the viral infection is an infection with a hepatitis virus.

78. (New) The method according to claim 74, wherein:

(a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA;

(b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO;

(c) at least 80% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA; and/or

(d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.

79. (New) The method according to claim 74, wherein the CD4⁺ helper T lymphocytes are derived from (a) CD45RA⁺ CD62L⁺ naïve T cell-enriched CD4⁺ population; (b) a CD45RO⁺ CD62L⁺ central memory T cell-enriched CD4⁺ population; (c) a CD45RA⁺ CD62L⁺ naïve T cell-enriched and CD45RO⁺ CD62L⁺ central memory T cell-enriched CD4⁺ population; or (d) a bulk CD4⁺ T cell population.

80. (New) The method according to claim 74, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody

fragment specific for an antigen associated with a disease or disorder, and an intracellular signaling module.

81. (New) The method according to claim 80, wherein the intracellular signaling module of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes, individually, comprise (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB costimulatory domain and a CD3 intracellular signaling domain.

82. (New) The method according to claim 74, wherein:

(a) the intracellular signaling domain of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;

(b) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;

(c) the intracellular signaling domain of the chimeric antigen receptor in the CD8⁺ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4⁺ T lymphocytes; or

(d) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is different than the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

83. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein:

(a) the intracellular signaling domain of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;

(b) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;

(c) the intracellular signaling domain of the chimeric antigen receptor in the CD8⁺ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4⁺ T lymphocytes; or

(d) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is different than the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

84. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the CD4⁺ helper T lymphocytes and the CD8⁺ cytotoxic T lymphocytes are derived from a subject and wherein:

(a) the CD4⁺ helper T lymphocytes secrete a greater amount of IL-2 and/or exhibit a greater degree of proliferation when cultured in the presence of the antigen as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory T cell-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;

(b) a greater percentage of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;

(c) a greater percentage of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD8⁺ T cell population or bulk CD8⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8⁺ cytotoxic T lymphocytes; and/or

(d) the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes proliferate when co-cultured *in vitro* with the CD4⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4⁺ T cells expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T

cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

85. (New) The adoptive cellular immunotherapy composition according to claim 39, wherein the CD4⁺ helper T lymphocytes and the CD8⁺ cytotoxic T lymphocytes are derived from a subject and wherein:

(a) the CD4⁺ helper T lymphocytes secrete a greater amount of IL-2 and/or exhibit a greater degree of proliferation when cultured in the presence of the antigen as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory T cell-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;

(b) a greater percentage of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;

(c) a greater percentage of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD8⁺ T cell population or bulk CD8⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8⁺ cytotoxic T lymphocytes; and/or

(d) the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes proliferate when co-cultured *in vitro* with the CD4⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4⁺ T cells expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

REMARKS

Favorable reconsideration of the present application in view of the above amendments and following remarks is respectfully requested. Claims 39-70 were pending in the application, of which claims 43, 48, 57 and 68 were withdrawn from consideration. As set forth above, Applicant has hereby canceled claims 41, 46, 51, 52, 55, 60, and 62-64 without prejudice to the filing of any divisional, continuation or continuation-in-part application thereon. Applicant expressly reserves the right to pursue canceled subject matter in continuing and divisional applications. Applicant has hereby amended claims 39, 40, 42-45, 47-50, 53, 54, 56-59, 61, and 65-70. Applicant hereby submits new claims 71-85. Support for amended and new claims may be found in the application as originally filed, for example, at page 3, lines 13-24; page 13, lines 18-26; page 16, lines 4-17; page 19, line 10-12; page 21, lines 30-33; Examples 4 and 5, Figures 9 and 10 (*see, e.g.*, claim 39); page 14, lines 11-22 (*see, e.g.*, claim 50, 70 and 79); page 6, lines 31-33; page 10, line 6 through page 11, line 4; page 12, lines 11-18; page 16, line 1 through page 17, line 9; page 21, line 33 through page 22, line 11; page 35, lines 20-30; page 38, lines 13-20 (*see, e.g.*, claim 84 and 85); page 11, lines 1-4; page 16, line 30 through page 17, line 2 (*see, e.g.*, claim 53); page 11, lines 1-4; page 16, line 30 through page 17, line 2 (*see, e.g.*, claims 41, 61, 69 and 78); page 18, lines 6-22 (*see, e.g.*, claims 58, 59, 71, 72, 80 and 81); page 19, lines 7-12 (*see, e.g.*, claims 47, 48, 73 and 82); page 18, line 28 through page 19, line 6 (*see, e.g.*, claims 40 and 54); and page 17, lines 18-21; page 25, lines 5-7; page 26, lines 9-10 (*see, e.g.*, claims 42, 43, 56, 57, 67 and 68). No new matter has been added. Upon entry of these amendments, claims 39, 40, 42-45, 47-50, 53, 54, 56-59, 61, and 65-85 will be pending.

Applicant acknowledges and thanks the Examiner for identifying claims 50 and 62 as being allowable if rewritten in independent form.

SPECIES ELECTION

Applicant acknowledges that the undersigned representative made a provisional species election during a telephone conversation with Examiner Michael D. Burkhart on April 21, 2016. Applicant confirms that the following provisional species elections were made: (1) antigen species of CD19 as recited in claim 42 and (b) the same signaling domain species as recited in claim 47.

In view of these species elections, Applicant requests consideration of claims to additional species that, written in independent form or otherwise, include all limitations of a later

allowed generic claim as provided by 37 C.F.R. §1.141(a). In this case, claims 43, 48, 57 and 68.

REJECTION UNDER 35 U.S.C. §102(b) AND §103(a) (PRE-AIA)

In the Office Action dated May 4, 2016, claims 39-42, 44-47, 49, 51-56, 58-61, 63-67, 69 and 70 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. §103(a) as allegedly obvious over, Huang *et al.* in view of Berger *et al.* and Sallusto *et al.* While the Examiner acknowledges that Huang *et al.* fail to teach CD8⁺ central memory T cells and CD4⁺ naïve T cells, the Examiner alleges that Berger *et al.* and Sallusto *et al.* teach a pool of T cells that inherently comprise such cells.

Applicant respectfully traverses this ground of rejection and submits that Huang *et al.*, Berger *et al.* and Sallusto *et al.*, taken individually alone or in any combination, fail to teach or suggest the currently claimed subject matter. The present claims are directed, in part, to an adoptive cellular immunotherapy composition containing chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein (a) the chimeric antigen receptor (CAR)-modified CD4⁺ T lymphocytes in the composition consist of helper T lymphocytes that contain a CAR that specifically binds to an antigen, and (b) the CAR-modified CD8⁺ T lymphocytes in the composition consist of CD8⁺ cytotoxic T lymphocytes that are derived from a central memory-enriched CD8⁺ cell population and contain a CAR that specifically binds to the antigen. The Examiner has not shown that Huang *et al.* teach or suggest, for example, a composition as claimed wherein the CAR-modified CD8⁺ T lymphocytes in the composition consist of CD8⁺ cytotoxic T lymphocytes that are derived from a central memory-enriched CD8⁺ cell population.

In the Office Action, the Examiner appears to allege that Huang *et al.* disclose the presently claimed compositions based on a theory that the recited populations were inherently present in the modified cells disclosed thereby. For example, the Examiner appears to allege that this composition necessarily contained CD62L⁺ CD4⁺ T cells based upon a description in Huang *et al.* that the majority of its CAR-modified T cells (about 95%) were CD4⁺ CD62L^{low} effector memory cells (at page 585, second column). The Examiner appears to have interpreted this disclosure as meaning the effector memory cells of Huang *et al.* are "CD62L⁺...absent a definitive definition." This conclusion is contrary to the definition of the instant specification and the common understanding in the art. The instant specification describes effector memory T

cells as not expressing or having decreased expression of CD62L on the surface thereof as compared to naïve or central memory T cells (*see* the published specification at paragraph [0032] and Fig. 8A). Further, Fig. 8A and paragraph [0040] of the instant specification indicate that naïve and central memory CD4⁺ T cells were CD62L⁺, compared with the CD62L⁻ (or low) effector population. Based upon at least this disclosure in the instant specification, and knowledge in the art, the Office has not established – nor would one of skill in the art assume – that Huang *et al.* described CD4⁺ T cells that were CD62L⁺. Nor does the Examiner cite anything in Huang *et al.* that would have taught or suggested a composition containing a CD8⁺ population as presently recited, such as one derived from central-memory enriched cells or containing any of the properties as presently recited. Accordingly, Applicant submits that the Examiner has not provided any evidence that Huang *et al.* necessarily taught or suggested a composition having CAR-modified CD62L⁺ T cells, or any of the an adoptive cellular immunotherapy compositions as claimed.

The disclosures of Berger *et al.* and Sallusto *et al.* do not remedy the deficiencies of Huang *et al.* Berger *et al.* and Sallusto *et al.* are alleged only to disclose general knowledge that T cell compositions can include various subpopulations that can be distinguished by the different cell surface markers the different cells express, and knowledge regarding surface markers expressed by CD8⁺ memory cells. Yet the mere existence of such T cell subpopulations or surface phenotypes would not support a conclusion that a composition as claimed inherently existed in the disclosure of Huang *et al.* or in any combination of the cited references.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). In other words, to support a finding of inherency, the evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference.... 'Inherency...may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (*citations omitted*). Thus, when "relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990); MPEP §2112(IV).

Here, the cited portion of Huang *et al.* states that the disclosed modified T cells are 95% CD4+ effector memory T cells and does not appear to specify which, if any, CD8+ T cell populations or types are present among the modified T cells or among cells used to derive them; nor has the Examiner pointed to any such disclosure. Even if certain other subpopulations were generally present in T cell compositions disclosed by other references, it would not necessarily follow that such a modified T cell population disclosed by Huang *et al.* is a composition containing CAR-modified CD4+ T lymphocytes that consist of helper T lymphocytes and CAR-modified CD8+ T lymphocytes that consist of CD8+ cytotoxic T lymphocytes derived from a central memory-enriched CD8+ cell population. Thus, Applicant submits that none of the references, taken alone or in any combination, teaches or suggests the claimed adoptive cellular immunotherapy composition or uses thereof.

In sum, Applicant respectfully submits the Examiner has neither established that Huang *et al.* teach every element of the claimed invention nor established a *prima facie* case of obviousness. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Favorable consideration and a Notice of Allowance are earnestly solicited. The Examiner is urged to contact the undersigned attorney if there are any questions prior to allowance of this matter.

Respectfully submitted,
SEED Intellectual Property Law Group LLP

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14/006,641	05/05/2014	Stanley R. Riddell	360056.420USPC	5681

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EXAMINER

BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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01/10/2017

PAPER

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.

Office Action Summary	Application No. 14/006,641	Applicant(s) RIDDELL ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	AIA (First Inventor to File) Status No

-- 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 10/4/2016.
☐ 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) 39, 40, 42-45, 47-50, 53, 54, 56-59, 61, 65--85 is/are pending in the application.
5a) Of the above claim(s) 43,48,57,68,74-82 and 85 is/are withdrawn from consideration.
- 6) ☒ Claim(s) 53,54,56,58,59,61,83 and 84 is/are allowed.
- 7) ☒ Claim(s) 39, 40, 42, 44, 45, 47, 49, 50, 65-67, 69 -73 is/are rejected.
- 8) ☐ Claim(s) ____ 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) | 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
Paper No(s)/Mail Date ____. | 4) ☐ Other: ____. |

Miltenyi Ex. 1008 Page 34

DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions.
Receipt and entry of the response dated 10/4/2016 is acknowledged.

Election/Restrictions

New claims 74-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species (the elected antigen, CD19, is a cancer antigen, not associated with infectious disease antigens), there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/4/2016.

Newly submitted claim 85 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claim 85 recites several distinct cell populations not linked by a special technical feature. The technical feature of, for example, the originally examined and currently examined claims (i.e. claim 39, considered to be Group I) is not a special technical feature because it is not a contribution over the prior art (see the 35 USC 102 rejections of record and below). As such, claim 85 is considered to contain 4 distinct Groups, or inventions, as found in sections (a)-(d) of the claim. The only technical feature linking these distinct cell populations is the cells population of claim 39, which is not a special technical feature for reasons above.

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (“requirement of unity of invention”). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression “special technical features” shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

WHEN CLAIMS ARE DIRECTED TO MULTIPLE CATEGORIES OF INVENTIONS

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

Art Unit: 1633

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

Restriction is required under 35 U.S.C. 121 and 372.

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.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 85 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 39, 40, 44, 50, 65, 66, 70, 71 is/are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Berger et al (Curr. Opin. Immunol., 2009, of record). **This is a new rejection necessitated by amendment of the claims.**

Berger et al teach CD4+ and CD8+ T-cells expressing tumor-specific CAR molecules wherein the CD8+ cells are T_{cm} (or T central memory cells). See in particular Fig. 3 and page 227, second column to page 229. The modified T cells are used in methods of treating cancer (abstract), including melanoma (page 227, first col., first full ¶). The CAR may comprise a single chain antibody fragment and an intracellular signaling molecule (page 229, first col).

Claim Rejections - 35 USC § 103

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under pre-AIA 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under pre-AIA 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of pre-AIA 35 U.S.C. 103(c) and potential pre-AIA 35 U.S.C. 102(e), (f) or (g) prior art under pre-AIA 35 U.S.C. 103(a).

Claim 39, 40, 42, 44, 45, 47, 49, 50, 65-67, 69 -73 is/are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Huang et al (2008, cited by applicants) in view of Berger et al (2009, cited by applicants), Berger et al (2008, cited by applicants) and Sallusto et al (2004, cited by applicants). **This is a new rejection necessitated by amendment of the claims.**

Huang et al teach a T cell composition comprising CD4+ and CD8+ cells expressing a CD19-specific chimeric antigen receptor (CAR) that in turn comprises a CD19 scFv, a transmembrane domain, a 4-1BB signaling domain and a CD3 intracellular domain. See, e.g. the abstract and Fig. 1a. Thus, both T cell subsets are considered to have the same intracellular signaling domain. The T cells used are considered autologous relative to the organism from which they were derived. The CAR T cells were used in methods of immunotherapy of CD19+ tumor cells (e.g., page 585).

Huang et al do not specifically teach that the CD8+ cells were derived from central memory enriched CD8+ cells, or have a certain percentage of CD62L+ CD8+ cells.

Art Unit: 1633

Berger et al (2008) teach CD4+ and CD8+ T-cells expressing tumor-specific CAR molecules wherein the CD8+ cells are T_{cm} (or T central memory cells) and there superior potential for adoptive T cell therapy. See in particular Fig. 3 and page 227, second column to page 229. The modified T cells are used in methods of treating cancer (abstract), including melanoma (page 227, first col., first full ¶). The CAR may comprise a single chain antibody fragment and an intracellular signaling molecule (page 229, first col).

Sallusto et al teach (e.g. Figure 1) that CD8+ memory cells are CD62L+ CD45RO+.

Berger et al (2009) teach techniques wherein up to 95% of CD8+ T_{cm} cells are CD62L+ (e.g. Fig. 1), and the superior properties of such cells for adoptive T cell transfer (e.g. abstract).

The claimed cells and methods are essentially disclosed by Huang et al with the exception of the CD8+ T_{cm} cell limitations. The ordinary skilled artisan, seeking a cell populations efficacious for treating, e.g., leukemia, would have been motivated to use CD8+ T_{cm} enriched cells with the methods of Huang et al because the Berger et al references (2008 and 2009) teach this subset to have well-known and desirable properties for adoptive T cell transfer. It would have been obvious for the skilled artisan to do this because of the known benefit of generating CAR-expressing T cells for administration in the treatment of cancers as taught by Berger and Huang et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

Claims 53,54,56,58,59,61,83 and 84 allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

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 an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/

Application/Control Number: 14/006,641

Page 9

Art Unit: 1633

Primary Examiner, Art Unit 1633

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Stanley R. Riddell *et al.*
Application No. : 14/006,641
Filed : May 5, 2014
For : METHOD AND COMPOSITIONS FOR CELLULAR
IMMUNOTHERAPY

Examiner : Michael D. Burkhart
Art Unit : 1633
Docket No. : 360056.420USPC
Date : June 12, 2017

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY AND AMENDMENT UNDER 37 C.F.R. §§1.116 AND 1.121

Commissioner for Patents:

Further to the Office Action dated January 10, 2017, please extend the time for response two (2) months, to expire on June 12, 2017 (which is timely filed since June 10, 2017 fell on a Saturday). Enclosed is a Petition for an Extension of Time, along with the requisite fee. Please enter into the record of the above-identified application the following:

Amendments to the Specification, which begin on page 2;

Amendments to the Claims, which are reflected in the Listing of Claims and begin on page 3 of this paper; and

Remarks, which begin on page 10 of this paper.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Amendments to the Specification

On page 1, please amend the paragraph beginning at line 15, as follows:

-- Statement Regarding Federally Sponsored Research

This invention was made with government support ~~in the form of grants R01CA18029 from the United States Department of Health and Human Services, under CA018029 awarded by the National Institutes of Health and Leukemia and Lymphoma Society SCORE grant.~~ The United States government has certain rights in the invention. --

Amendments to the Claims

Please cancel claims 39, 40, 42-45, 47-50, 57, 65-82, and 85 without prejudice; amend claims 56, 58, 83 and 84; and add new claims 86-108, as shown below. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. – 52. (Canceled)

53. (Previously Presented) An adoptive cellular immunotherapy composition containing chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein:

(a) the chimeric antigen receptor-modified CD4⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to an antigen and at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or CD45RA, and

(b) the chimeric antigen receptor-modified CD8⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to the antigen and at least 50% of CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L and/or CD45RO.

54. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is associated with a disease or disorder selected from a solid tumor, hematologic malignancy, melanoma, and infection with a pathogen.

55. (Canceled)

56. (Currently Amended) The adoptive cellular immunotherapy composition according to ~~claims claim~~ 53, wherein the antigen is selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA.

57. (Canceled)

58. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody fragment specific for ~~an~~ the antigen ~~associated with a disease or disorder~~, and an intracellular signaling module.

59. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 58, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes, individually, comprise (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB costimulatory domain and a CD3 intracellular signaling domain.

60. (Canceled)

61. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein:

(a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA;

(b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO;

(c) at least 80% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA; and/or

(d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.

62. – 82. (Canceled)

83. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein:

(a) the intracellular signaling domain of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;

~~(b) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4⁺ T lymphocytes;~~

~~(c) the intracellular signaling domain of the chimeric antigen receptor in the CD8⁺ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4⁺ T lymphocytes; or~~

~~(d) the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is different than the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.~~

84. (Currently Amended) The adoptive cellular immunotherapy composition according to claim 53, wherein the CD4⁺ helper T lymphocytes and the CD8⁺ cytotoxic T lymphocytes are derived from a subject and wherein:

(a) the CD4⁺ helper T lymphocytes secrete a greater amount of IL-2 and/or exhibit a greater degree of proliferation when cultured in the presence of the antigen as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory T cell-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;

~~(b) a greater percentage of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes;~~

~~(c) a greater percentage of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8⁺ T cells that has been expanded *in vitro* from an effector memory-enriched~~

~~CD8⁺ T-cell population or bulk CD8⁺ T-cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8⁺ cytotoxic T lymphocytes; and/or~~

~~(d) the chimeric antigen receptor modified CD8⁺ cytotoxic T lymphocytes proliferate when co-cultured *in vitro* with the CD4⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4⁺ T cells expanded *in vitro* from an effector memory enriched CD4⁺ T-cell population or a bulk CD4⁺ T-cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.~~

85. (Canceled)

86. (New) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L.

87. (New) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

88. (New) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and at least 50% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

89. (New) The adoptive cellular immunotherapy composition of claim 53, wherein at least 60% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

90. (New) The adoptive cellular immunotherapy composition of claim 53, wherein at least 80% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

91. (New) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition and the the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are present in the composition at a ratio of between about 2:1 to about 1:2.

92. (New) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition and the the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are present in the composition at a ratio of about 2:1, 1:1, or 1:2.

93. (New) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

94. (New) The adoptive cellular immunotherapy composition of claim 53, wherein the intracellular signaling domain of the chimeric antigen receptor in the CD8⁺ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen receptor in the CD4⁺ T lymphocytes; or the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is different than the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

95. (New) The adoptive cellular immunotherapy composition according to claims 53, wherein the antigen is ROR1.

96. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is Her2.

97. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is L1-CAM.

98. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD19.

99. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD20.

100. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD22.

101. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is mesothelin.

102. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CEA.

103. (New) The adoptive cellular immunotherapy composition according to claim 54, wherein the disease or disorder is a solid tumor, hematologic malignancy, or melanoma.

104. (New) The adoptive cellular immunotherapy composition according to claim 54, wherein the disease or disorder is a hematologic malignancy.

105. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is a tumor associated antigen associated with a cancer selected from the

group consisting of melanoma, breast cancer, squamous cell carcinoma, colon cancer, leukemia, myeloma, prostate cancer, B cell lymphoma, breast cancer, prostate cancer, and leukemia.

106. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein a greater percentage of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

107. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein a greater percentage of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD8⁺ T cell population or bulk CD8⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8⁺ cytotoxic T lymphocytes.

108. (New) The adoptive cellular immunotherapy composition according to claim 53, wherein the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes proliferate when co-cultured *in vitro* with the CD4⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4⁺ T cells expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

REMARKS

Favorable reconsideration of the present application in view of the above amendments and following remarks is respectfully requested. Claims 39, 40, 42-45, 47-50, 53, 54, 56-59, 61, and 65-85 were pending in the application. As shown above, Applicant has hereby amended claims 56, 58, 83 and 84; and canceled claims 39, 40, 42-45, 47-50, 57, 65-82, and 85.

Applicant notes that amendments to and/or cancelation of claims have been made without acquiescence, prejudice, or disclaimer and solely for the purpose of expediting prosecution. Applicant expressly reserves the right to pursue canceled subject matter in continuing and divisional applications. Applicant has hereby added new claims 86-108. Support for the amendments can be found throughout the application as originally filed. See, for example, pending claim 53 (*see, e.g.*, claims 86-88); pending claim 54; at page 17, lines 10-21 and page 26, lines 15-24 (*see, e.g.*, claims 86-88); pending claim 56 (*see, e.g.*, claims 95-102); pending claim 61 (*see, e.g.*, claims 89 and 90); pending claim 83 (*see, e.g.*, claims 93 and 94); pending claim 84 (*see, e.g.*, claims 106-108); and page 34, lines 4-9; page 36, lines 6-21; and page 42, lines 9-14 (*see, e.g.*, claims 91 and 92). Upon entry of these amendments, claims 53, 54, 56, 58, 59, 61, 83, 84 and 86-108 will be pending.

ALLOWABLE SUBJECT MATTER

In the Office Action dated January 10, 2017, claims 53, 54, 56, 58, 59, 61, 83 and 84 were allowed. Applicant thanks the Examiner for identifying the allowable subject matter. In this regard, Applicant has hereby canceled without prejudice or disclaimer the claims that were not yet deemed allowable (*i.e.*, claims 39, 40, 42-45, 47-50, 57, 65-82, and 85). In addition, Applicant has hereby added new claims 86-108, which generally include subgeneric and/or species claims of previous pending claims 53, 54, 56, 61, 83 and 84, as set forth above. New claims 91 and 92 depend from allowed claim 53 and recite ratios of chimeric antigen receptor (CAR)-modified CD4⁺ helper T lymphocytes to CAR-modified CD8⁺ cytotoxic T lymphocytes as described in the instant specification (*see, e.g.*, specification at page 34, lines 4-9; page 36, lines 6-21; and at page 42, lines 9-14). Accordingly, Applicant respectfully requests that new claims 86-108 be allowed together with allowed claims 53, 54, 56, 58, 59, 61, 83 and 84.

REJECTION UNDER 35 U.S.C. §102(b) (PRE-AIA)

In the Office Action dated January 10, 2017, claims 39, 40, 44, 50, 65, 66, 70 and 71 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Berger *et al.* (*Curr. Opin. Immunol.*, 2009). Applicant submits that this rejection has been rendered moot since the above-noted rejected claims have been canceled without prejudice or disclaimer. Accordingly, Applicant requests that this ground of rejection be withdrawn.

REJECTION UNDER 35 U.S.C. §103(a) (PRE-AIA)

In the Office Action, claims 39, 40, 42, 44, 45, 47, 49, 50, 65-67 and 69-73 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Huang *et al.* (*Mol. Ther.* 16:580, 2008), in view of Berger *et al.* (2009), Berger *et al.* (*J. Clin. Invest.* 118:294, 2008), and Sallusto *et al.* (*Ann. Rev. Immunol.* 22:745, 2004). Applicant submits that this rejection has been rendered moot since the above-noted rejected claims have been canceled without prejudice or disclaimer. Accordingly, Applicant requests that this ground of rejection be withdrawn.

CONCLUSION

In view of the above, Applicant believes that presently pending claims 53, 54, 56, 58, 59, 61, 83, 84 and 86-108 are in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited. The Examiner is urged to contact the undersigned attorney if there are any questions prior to allowance of this matter.

Respectfully submitted,
SEED Intellectual Property Law Group LLP

/Jeffrey C. Pepe/
Jeffrey C. Pepe, Ph.D.
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/006,641	05/05/2014	Stanley R. Riddell	360056.420USPC	5681

500 7590 07/25/2017
SEED INTELLECTUAL PROPERTY LAW GROUP LLP
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER

BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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07/25/2017

PAPER

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.

Office Action Summary	Application No. 14/006,641	Applicant(s) RIDDELL ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	AIA (First Inventor to File) Status No

-- 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 7/10/2017.
☐ 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) 53,54,56,58,59,61,83,84 and 86-108 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) 53, 54, 56, 58, 59, 61, 83, 84, 86-108 is/are rejected.
- 8) ☐ Claim(s) ____ 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 7/10/2017.
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 4) ☐ Other: ____.

Miltenyi Ex. 1008 Page 55

DETAILED ACTION

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/2017 has been entered.

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 §§ 706.02(l)(1) - 706.02(l)(3) 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 USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The 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/process/file/efs/guidance/eTD-info-I.jsp.

Claims 53, 54, 56, 58, 59, 61, 83, 84, 86-108 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 74-78 of copending Application No. 14/422,640 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the '640 application also claims a composition comprising CD4+ and CD8+ T cells expressing a CAR, which, according to the '640 specification (e.g. pages 18-19, 42-43, 48), have the instantly recited surface markers. Further,

Art Unit: 1633

other dependent claim limitations are found to be preferred embodiments in the '640 specification.

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 Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

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 an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Stanley R. Riddell *et al.*
Application No. : 14/006,641
Filed : May 5, 2014
For : METHOD AND COMPOSITIONS FOR CELLULAR
IMMUNOTHERAPY

Examiner : Michael D. Burkhart
Art Unit : 1633
Docket No. : 360056.420USPC
Date : October 25, 2017

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY AND AMENDMENT UNDER 37 C.F.R. §§1.111 AND 1.121

Commissioner for Patents:

Further to the Office Action dated July 25, 2017, please enter into the record of the above-identified application the following:

Amendments to the Claims are reflected in the Listing of Claims beginning on page 2 of this paper; and

Remarks, which begin on page 9 of this paper.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Amendments to the Claims

Claims 91 and 92 have been amended, as shown below. This Listing of Claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims

1. – 52. (Canceled)

53. (Previously Presented) An adoptive cellular immunotherapy composition containing chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein:

(a) the chimeric antigen receptor-modified CD4⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to an antigen and at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or CD45RA, and

(b) the chimeric antigen receptor-modified CD8⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to the antigen and at least 50% of CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L and/or CD45RO.

54. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is associated with a disease or disorder selected from a solid tumor, hematologic malignancy, melanoma, and infection with a pathogen.

55. (Canceled)

56. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA.

57. (Canceled)

58. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody fragment specific for the antigen and an intracellular signaling module.

59. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 58, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes, individually, comprise (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB costimulatory domain and a CD3 intracellular signaling domain.

60. (Canceled)

61. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein:

(a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA;

(b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO;

(c) at least 80% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA; and/or

(d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.

62. – 82. (Canceled)

83. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the intracellular signaling domain of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

84. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the CD4⁺ helper T lymphocytes and the CD8⁺ cytotoxic T lymphocytes are derived from a subject and wherein the CD4⁺ helper T lymphocytes secrete a greater amount of IL-2 and/or exhibit a greater degree of proliferation when cultured in the presence of the antigen as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory T cell-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

85. (Canceled)

86. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L.

87. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

88. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and at least 50% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

89. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein at least 60% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

90. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein at least 80% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

91. (Currently Amended) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition and ~~the~~ the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are present in the composition at a ratio of between about 2:1 to about 1:2.

92. (Currently Amended) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition and ~~the~~ the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are present in the composition at a ratio of about 2:1, 1:1, or 1:2.

93. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.

94. (Previously Presented) The adoptive cellular immunotherapy composition of claim 53, wherein the intracellular signaling domain of the chimeric antigen receptor in the CD8⁺ T lymphocytes is different from the intracellular signaling domain of the chimeric antigen

receptor in the CD4+ T lymphocytes; or the chimeric antigen receptor contained by the CD8+ T lymphocytes is different than the chimeric antigen receptor contained by the CD4+ T lymphocytes.

95. (Previously Presented) The adoptive cellular immunotherapy composition according to claims 53, wherein the antigen is ROR1.

96. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is Her2.

97. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is L1-CAM.

98. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD19.

99. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD20.

100. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CD22.

101. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is mesothelin.

102. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is CEA.

103. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 54, wherein the disease or disorder is a solid tumor, hematologic malignancy, or melanoma.

104. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 54, wherein the disease or disorder is a hematologic malignancy.

105. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the antigen is a tumor associated antigen associated with a cancer selected from the group consisting of melanoma, breast cancer, squamous cell carcinoma, colon cancer, leukemia, myeloma, prostate cancer, B cell lymphoma, breast cancer, prostate cancer, and leukemia.

106. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein a greater percentage of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

107. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein a greater percentage of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8⁺ T cells that has been expanded *in vitro* from an effector memory-enriched CD8⁺ T cell population or bulk CD8⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8⁺ cytotoxic T lymphocytes.

108. (Previously Presented) The adoptive cellular immunotherapy composition according to claim 53, wherein the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes proliferate when co-cultured *in vitro* with the CD4⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4⁺ T cells expanded *in vitro* from an effector memory-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.

REMARKS

Reconsideration of the present application in view of the following remarks is respectfully requested. Claims 53, 54, 56, 58, 59, 61, 83, 84 and 86-108 are pending. Applicant has hereby amended claims 91 and 92 to correct an inadvertent typographical error. No new matter has been added. Upon entry of this amendment, claims 53, 54, 56, 58, 59, 61, 83, 84 and 86-108 will remain pending.

REJECTION UNDER OBVIOUSNESS-TYPE DOUBLE PATENTING

In the Office Action dated July 25, 2017, claims 53, 54, 56, 58, 59, 61, 83, 84 and 86-108 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 74-78 of co-pending USAN 14/422,640 ('640 application).

Applicant respectfully traverses this ground of rejection and submits that the instant claims do not conflict with claims 74-78 of the '640 application. Regardless, without acquiescing, Applicant notes that this non-statutory double patenting rejection is the only rejection remaining in the instant Office Action, and the instant application has an earlier effective U.S. filing date than the '640 application (*i.e.*, March 23, 2011 versus August 20, 2012). Under these circumstances, MPEP §804(I)(B)(1) provides that the Examiner should withdraw the rejection in the application having the earliest effective U.S. filing date and permit that application to issue as a patent. Furthermore, MPEP §804(I)(B)(1) provides that a terminal disclaimer need not be filed in the application with the earliest effective U.S. filing date when a non-statutory double patenting rejection is raised between two applications – as is the case here.

Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Application No. 14/006,641
Reply to Office Action dated July 25, 2017

Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
SEED Intellectual Property Law Group LLP

/Jeffrey C. Pepe/
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NOTICE OF ALLOWANCE AND FEE(S) DUE

500 7590 01/30/2018
SEED INTELLECTUAL PROPERTY LAW GROUP LLP
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER

BURKHART, MICHAEL D

ART UNIT

PAPER NUMBER

1633

DATE MAILED: 01/30/2018

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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14/006,641

05/05/2014

Stanley R. Riddell

360056.420USPC

5681

TITLE OF INVENTION: METHOD AND COMPOSITIONS FOR CELLULAR IMMUNOTHERAPY

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$500	\$0	\$0	\$500	04/30/2018

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 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity 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 and an extra copy of the form should be submitted. 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), to: **Mail** **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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 including the Patent, advance orders and notification of maintenance fees 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.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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.

500 7590 01/30/2018
SEED INTELLECTUAL PROPERTY LAW GROUP LLP
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

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 facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/006,641	05/05/2014	Stanley R. Riddell	360056.420USPC	5681

TITLE OF INVENTION: METHOD AND COMPOSITIONS FOR CELLULAR IMMUNOTHERAPY

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$500	\$0	\$0	\$500	04/30/2018

EXAMINER	ART UNIT	CLASS-SUBCLASS
BURKHART, MICHAEL D	1633	424-184100

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/SB/122) attached. ☐ "Fee Address" indication (or "Fee Address" Indication form 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, 1 _____ (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. 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 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.

(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. The following fee(s) are submitted: ☐ Issue Fee ☐ Publication Fee (No small entity discount permitted) ☐ Advance Order - # of Copies _____	4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above) ☐ A check is enclosed. ☐ Payment by credit card. Form PTO-2038 is attached. ☐ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).
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5. Change in Entity Status (from status indicated above)

- ☐ Applicant certifying micro entity status. See 37 CFR 1.29
- ☐ Applicant asserting small entity status. See 37 CFR 1.27
- ☐ Applicant changing to regular undiscounted fee status.

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.

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.

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. _____

Miltenyi Ex. 1006 Page 70



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/006,641	05/05/2014	Stanley R. Riddell	360056.420USPC	5681

500 7590 01/30/2018
SEED INTELLECTUAL PROPERTY LAW GROUP LLP
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER

BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 01/30/2018

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 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, 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, local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 14/006,641	Applicant(s) RIDDELL ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	AIA (First Inventor to File) Status No

-- 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 10/25/2017.
☐ 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 53,54,56,58,59,61,83,84 and 86-108. 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) | 5. ☐ Examiner's Amendment/Comment |
| 2. ☐ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 6. ☒ Examiner's Statement of Reasons for Allowance |
| 3. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 7. ☐ Other _____. |
| 4. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____. | |

/Michael Burkhart/
Primary Examiner, Art Unit 1633

Art Unit: 1633

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance: the prior art does not teach or suggest the combination of CD4+ and CD8+ T cells as instantly claimed. Specifically, the use of CD4+ T cells that are the required % positive for CD62L or CD45RA is not taught. Rather, many prior art references teach preparing CAR cells from CD8+ cells only (e.g. Berger et al 2008), or that the subset of CD4+ cells to be used was unknown at the time of the invention (e.g. Berger et al 2009, page 228, second col).

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."

/Michael Burkhart/

Primary Examiner, Art Unit 1633