

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.,
Petitioner,

v.

10X GENOMICS, INC.,
Patent Owner.

Case No. IPR2023-00876
U.S. Patent No. 10,155,981

**PETITIONER'S SUPPLEMENTAL PAPER IN SUPPORT OF
SUBMISSION OF DR. QUACKENBUSH REPORT EXCERPT**

PETITIONER’S UPDATED EXHIBIT LIST

Exhibit #	Description
EX1001	U.S. Patent No. 10,155,981 (the “’981 patent”)
EX1002	Declaration of Gregory Cooper, Ph.D.
EX1003	PCT Patent Publication No. WO 2010/117620 to Linnarsson et al. (“Linnarsson”)
EX1004	Megan L McCloskey et al., <i>Encoding PCR Products with Batch-Stamps and Barcodes</i> , 45 Biochemical Genetics, 761-767 (2007) (“McCloskey”)
EX1005	Prosecution File History of U.S. Patent No. 10,155,981
EX1006	Leslie H. Brail et al., <i>Gene expression in individual cells: analysis using global single cell reverse transcription polymerase chain reaction (GSC RT-PCR)</i> , 406 Mutation Research Genomics, 45-54 (1999) (“Brail”)
EX1007	Hubert Hug et al., <i>Measurement of Number of Molecules of a Single mRNA Species in a Complex mRNA Preparation</i> , 221 J. Theor. Bio., 615-624 (2003) (“Hug”)
EX1008	Heather D. VanGuilder et al., <i>Twenty-five years of quantitative PCR for gene expression analysis</i> , 44 BioTechniques, 619-626 (2008) (“VanGuilder”)
EX1009	Gerald Schochetman et al., <i>Polymerase Chain Reaction</i> , 158 J. of Infectious Diseases 1154-1157 (1988) (“Schochetman”)
EX1010	Silvia G. Acinas et al., <i>PCR-Induced Sequence Artifacts and Bias: Insights from Comparison of Two 16S rRNA Clone Libraries Constructed from the Same Sample</i> , 17 Applied and Environmental Microbiology 8966-8969 (2005) (“Acinas”)
EX1011	H.C. Yang et al., <i>A genome-wide study of preferential amplification/hybridization in microarray-based pooled DNA experiments</i> , 34 Nucleic Acids Research 1-11 (2006) (“Yang”)

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EX1012	Severine A Degrelle et al., <i>Amplification biases: possible difference among deviating gene expressions</i> , 9 BMC Genomics 1-15 (2008) (“Degrelle”)
EX1013	Brooks E. Miner et al., <i>Molecular barcodes detect redundancy and contamination in hairpin-bisulfite PCR</i> , 32 Nucleic Acids Research 1-4 (2004) (“Miner”)
EX1014	U.S. Patent No. 8,298,767 B2
EX1015	U.S. Patent Provisional Application No. 61/164,759 (filed March 30, 2009) (Sven Linnarsson, applicant) (“Linnarsson Provisional”)
EX1016	Defendant 10X Genomic’s Opening Brief In Support Of Its Motion To Dismiss, <i>Becton, Dickinson and Company and Cellular Research, Inc. v. 10X Genomics, Inc.</i> , C.A. No. 18-1800-RGA (Mar. 1, 2019 D. Del.) (No. 19)
EX1017	Defendant 10X Genomic’s Reply Brief In Support Of Its Motion To Dismiss, <i>Becton, Dickinson and Company and Cellular Research, Inc. v. 10X Genomics, Inc.</i> , C.A. No. 18-1800-RGA (Apr. 12, 2019 D. Del.) (No. 22)
EX1018	Scheduling Order, <i>10X Genomics, Inc. and The Board of Trustees of the Leland Stanford Junior University v. Parse Biosciences, Inc.</i> , C.A. No. 22-1117-JHS (Mar. 2, 2023 D. Del.) (No. 48)
EX1019	Federal Judicial Caseload Statistics (2022), at https://www.uscourts.gov/statistics-reports/analysis-reports/federal-judicial-caseload-statistics
EX1020	Curriculum Vitae of Gregory Cooper
EX1021	Jonas Binladen et al., <i>The Use of Coded PCR Primers Enables High Throughput Sequencing of Multiple Homolog Amplification Products by 454 Parallel Sequencing</i> , 2(2): e197 PLoS ONE 1-9 (2007) (Binladen)
EX1022	S. Kwok et al., <i>Effects of primer-template mismatches on the polymerase chain reaction: Human immunodeficiency virus type 1 model studies</i> , 18 Nucleic Acids Research 999-1005 (1990) (“Kwok”)

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EX1023	Motion Success for Stay Pending IPR In Delaware District
EX1024	Hiroto Okayama and Paul Berg, <i>High-Efficiency Cloning of Full-Length cDNA</i> , 2 Molecular and Cellular Biology 161-170 (1982) (“Okayama”)
EX1025	Bruce Alberts, et al., “Chapter 6 How Cells read the Genome: From DNA To Protein,” <i>Molecular Biology of the Cell</i> , Garland Science 299-335 (4th ed. 2002)
EX1026	Assignment Record for U.S. Patent 8,298,767
EX1027	10x Genomics Legal Notice
EX1028	Declaration of Sylvia D. Hall-Ellis, Ph.D.
EX1029	US Patent No. 8,835,358 B2
EX1030	S. Clancy et al., <i>Translation: DNA to mRNA to Protein</i> , Nature Education (2008), at https://www.nature.com/scitable/topicpage/translation-dna-to-mrna-to-protein-393/
EX1031	Cole Trapnell, <i>Defining cell types and states with single-cell genomics</i> , 25(10) Genome Research 1491-1498 (2015) (“Trapnell”)
EX1032	Gerard Brady et al., <i>Representative in Vitro cDNA Amplification From Individual Hemopoietic Cells and Colonies</i> , 2 Methods in Molecular and Cellular Biology 17-25 (1990) (“Brady”)
EX1033	James Eberwine et al., <i>Analysis of gene expression in single live neurons</i> , 89 Proc. Natl. Acad. Sci. 3010-3014 (1992) (“Eberwine”)
EX1034	Maria de Fatima Bonaldo et al., <i>Normalization and Subtraction: Two Approaches to Facilitate Gene Discovery</i> , 6(9) Genome Research 791-806 (1996) (“Bonaldo”)
EX1035	Sydney Brenner et al., <i>In vitro cloning of complex mixtures of DNA on microbeads: Physical separation of differentially expressed cDNAs</i> , 97.4 Proceedings of the Nat’l Academy of Sci. 1665-1670 (2000) (“Brenner”)

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EX1036	David H. Persing, <i>Polymerase Chain Reaction: Trenches to Benches</i> , J. of Clinical Microbiology 1281-1285 (1991) (“Persing”)
EX1037	Kazuki Kurimoto et al., <i>An improved single-cell cDNA amplification method for efficient high-density oligonucleotide microarray analysis</i> , 34(5) Nucleic Acids Research 1-17 (2006) (“Kurimoto”)
EX1038	Shigeyuki Esumi et al., <i>Method for single-cell microarray analysis and application to gene-expression profiling of GABAergic neuron progenitors</i> , 60 Neuroscience Research 439-451 (2008) (“Esumi”)
EX1039	Y. Shibata et al., <i>Cloning Full-length, Cap-Trapper-Selected cDNAs by Using the Single-Strand Linker Ligation Method</i> , 30(6) Biotechniques 1250-1254 (2001) (“Shibata”)
EX1040	U.S. Patent Application 2004/0166499
EX1041	Athina Gkazi, <i>An Overview of Next-Generation Sequencing</i> , Technology Networks Genomics Research at Figure 2 (March 17, 2021) at https://www.technologynetworks.com/genomics/articles/an-overview-of-next-generation-sequencing-346532
EX1042	Rami Sukarieh, <i>Relocalization of eIF4E by its binding partners upon stress</i> , Figure 2 (August 2009) at https://www.researchgate.net/publication/41663010_Relocalization_of_eIF4E_by_its_binding_partners_upon_stress
EX1043	Clyde A. Hutchinson, <i>DNA sequencing: bench to bedside and beyond</i> , 35(18) Nucleic Acids Research 6227-6237 (2007) (“Hutchinson”)
EX1044	Beáta G Vértessy and Judit Tóth, <i>Keeping Uracil Out of DNA: Physiological Role, Structure and Catalytic Mechanism of dUTPases</i> , Acc Chem Res. 1-20 (2009) (“Vértessy”)
EX1045	Elaine R. Mardis, <i>Next-Generation DNA Sequencing Methods</i> , 9 Annual Review Genomics and Human Genetics 387-402 (2008) (“Mardis”)
EX1046	Jay Shendure and Hanlee Ji, <i>Next-Generation DNA Sequencing</i> , 26(10) Nature Biotechnology 1135-1145 (2008) (“Shendure”)

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EX1047	Elaine R. Mardis, <i>The impact of next-generation sequencing technology on genetics</i> , 24(3) Trends in Genetics 133-141 (2008) (“Mardis 2”)
EX1048	Robert A. Holt and Steven J.M. Jones, <i>The new paradigm of flow cell sequencing</i> , 18(6) Genome Research 839-846 (2008) (“Holt”)
EX1049	National Human Genome Research Institute, <i>Nucleotide</i> (March 21, 2023) at https://www.genome.gov/genetics-glossary/Nucleotide
EX1050	National Human Genome Research Institute, <i>Polymerase Chain Reaction</i> (March 21, 2023) at https://www.genome.gov/genetics-glossary/Polymerase-Chain-Reaction
EX1051	Plaintiffs, Becton, Dickinson and Company and Cellular Research, Inc.’s First Amended Complaint, <i>Becton, Dickinson and Company and Cellular Research, Inc. v. 10X Genomics, Inc.</i> , C.A. No. 18-1800-RGA (Feb 08, 2019 D. Del.) (No. 15)
EX1052	Exhibits 26 and 27 attached with Plaintiffs’ First Amended Complaint, <i>Becton, Dickinson and Company and Cellular Research, Inc. v. 10X Genomics, Inc.</i> , C.A. No. 18-1800-RGA (Feb 08, 2019 D. Del.) (No. 15-3)
EX1053	US Patent No. 9,708,659 B2
EX1054	Declaration of Edward R. Reines in support of pro hac vice motion
EX1055	<i>In re Reines</i> Federal Circuit decision, 14-MA0004
EX1056	Personal Statement of Edward R. Reines, Fed. Cir. 14-MA004
EX1057	The transcript of the deposition of John Quackenbush, Ph.D., taken on February 28, 2024
EX1058	Joint Claim Construction Brief, <i>10X Genomics, Inc. and The Board of Trustees of the Leland Stanford Junior University v. Parse Biosciences, Inc.</i> , C.A. No. 22-1117-JHS (Dec 7, 2023 D. Del.) (No. 104)
EX1059	Declaration of Gregory Cooper, Ph.D. in Support of Petitioner’s Reply to Patent Owner’s Response

Exhibit #	Description
EX1060	U.S. Patent No. 10,240,197 B1
EX1061	Moran, Mary Ann, et al., <i>Sizing up metatranscriptomics</i> , The ISME Journal, vol. 7, pp. 237-243 (2013)
EX1062	Ball, Philip, <i>Smallest genome clocks in at 182 genes</i> , Nature (Oct. 12, 2006)
EX1063	Perez-Ortin, Jose, E., et al., <i>A genomic view of mRNA turnover in yeast</i> , C.R. Biologies, vol. 334 pp. 647-654 (2011)
EX1064	New England BioLabs webpage, BtsCI Product Information, available at https://www.neb.com/en-us/products/r0647-btsci
EX1065	Declaration of Sylvia D. Hall-Ellis, Ph.D.
EX1066	Opinion regarding Claim Construction, D.I. 209
EX1067	Excerpted Opening Report of John Quackenbush, Ph.D., served on May 17, 2024 – REDACTED

Pursuant to the Board’s June 20, 2024 order, Petitioner submits this paper documenting how 10x’s expert, Dr. John Quackenbush, has taken directly contrary positions regarding the term “sequencing the plurality of tagged polynucleotides” in this tribunal and in parallel district court proceedings.

In this IPR, Dr. Quackenbush has opined that this term requires sequencing the “entirety” of a “tagged polynucleotide.” Specifically, Dr. Quackenbush has opined that Petitioner’s expert, Dr. Gregory Cooper, did not establish that Linnarsson teaches the “sequencing” claim element because Dr. Cooper did not show “how Linnarsson’s sequencing of only a portion of each tagged polynucleotide, as opposed to the entirety of the tagged polynucleotides, could satisfy this limitation.” EX2013 ¶ 54 (emphasis in original). Petitioner has relied upon these opinions that the claim require sequencing the “entirety” of the tagged polynucleotides as a key aspect of its rebuttal to the Petition. *See* POR at 23-25.

In parallel district court proceedings, however, Dr. Quackenbush has disavowed any suggestion that “sequencing the plurality of tagged polynucleotides” requires sequencing the “entirety” of the tagged polynucleotides. As Dr. Quackenbush stated, the “claims ***do not*** require sequencing the entirety of the tagged polynucleotides.” EX1067 ¶ 161 (emphasis added).

These contrasting positions speak to the deficiencies in Patent Owner’s response to the Petition.

Dated: June 25, 2024

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing **PETITIONER’S
SUPPLEMENTAL PAPER IN SUPPORT OF SUBMISSION OF DR.
QUACKENBUSH REPORT EXCERPT** is being served on June 25, 2024, via
electronic mail pursuant to 37 C.F.R. § 42.6(e) to the counsel for Patent Owner at
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