

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Petitioner

v.

THE CHINESE UNIVERSITY OF HONG KONG,
Patent Owner

PTAB Case No. **IPR2024-00028**
U.S. Patent No. **11,091,794 B2**

**SUBMISSION OF EXHIBITS 2061 AND 2062
AND UPDATED EXHIBIT LIST**

Confidential Exhibits 2061 and 2062 are submitted herewith and designated
as:

PARTIES AND BOARD ONLY:

Ex. 2061	CONFIDENTIAL - PacBio – CUHK Assignment and Settlement Agreement.
Ex. 2062	CONFIDENTIAL - PacBio – Take2 Mutual Release

Pursuant to 37 C.F.R. § 42.63(e), a current Exhibit List follows.

LIST OF EXHIBITS

Petitioner's Exhibits	
No.	Description
1001	U.S. Patent No. 11,091,794 to Lo ("the '794 patent")
1002	Declaration of Dr. Christophe Dessimoz
1003	Curriculum Vitae of Christophe Dessimoz, Ph.D.
1004	U.S. Patent Application No. 16/995,607 File History
1005	U.S. Patent Application No. 17/379,544 File History
1006	Flusberg, et al., "Direct Detection of DNA Methylation During Singlemolecule, Real-Time Sequencing," Nature Methods 7(6) (2010) ("Flusberg")
1007	U.S. Patent No. 9,175,338 to Flusberg et al. ("Flusberg-338")
1008	Clark, et al. "Direct Detection and Sequencing of Damaged DNA Bases" Genome Integrity 2 (2011) ("Clark")
1009	Loomis et al., "Sequencing the Unsequenceable: Expanded CGG-repeat Alleles of the Fragile X Gene," Genome Research 23(1) (2013) ("Loomis")
1010	Schadt, et al., "Modeling Kinetic Rate Variation in Third Generation DNA Sequencing Data to Detect Putative Modifications to DNA Bases," Genome Research 23(1) (2013) ("Schadt")
1011	BAM Format Specification for PacBio, PacBioFileFormats 5.0 Documentation, http://web.archive.org/web/20170916112547/http://pacbiofileformats.readthedocs.io/en/5.0/BAM.html (archived Sep. 16, 2017) ("PacBio-BAM")

Petitioner's Exhibits	
No.	Description
1012	SAM/BAM Specification Working Group, Sequence Alignment/Map Format Specification, http://web.archive.org/web/20180613134937/http://samtools.github.io/hts-specs/SAMv1.pdf (archived Jun. 13, 2018) ("SAM/BAM Specification")
1013	Davis et al., "Entering the Era of Bacterial Epigenomics with Single Molecule Real Time DNA Sequencing," Current Opinion in Microbiology, 16(2) (2013) ("Davis")
1014	Take2 Tech, Ltd. v. Pac. Biosciences of Cal., Inc., DDE-1-22-cv-01595, Infringement Claim Chart for U.S. Patent No. 11,091,794 ("Take2 Infringement Contentions")
1015	Feng, et al, "Detecting DNA modifications from SMRT Sequencing Data by Modeling Sequence Context Dependence of Polymerase Kinetic," PLoS Computational Biology, 9(3) (2013) ("Feng")
1016	"Detecting DNA Base Modifications Using Single Molecule, Real-Time Sequencing," https://www.pacb.com/wp-content/uploads/2015/09/WP_Detecting_DNA_Base_Modifications_Using_SMRT_Sequencing.pdf (2012) ("PacBio White Paper")
1017	Zou et al., "A Primer on Deep Learning in Genomics" Nature Genetics, 51(1) (Jan. 2019)
1018	U.S. Patent Pub. No. 2016/0326593 to Clement et al. ("Clement")
1019	Pacific Biosciences Template Preparation and Sequencing Guide, https://www.pacb.com/wp-content/uploads/2015/09/Guide-Pacific-Biosciences-Template-Preparation-and-Sequencing.pdf (2015) ("PacBio Template Guide")
1020	U.S. Patent Publication No. 2016/0208241 to Tsai et al. ("Tsai")

Petitioner's Exhibits	
No.	Description
1021	Pacific Biosciences kineticsTools Manual, http://web.archive.org/web/20170813085437/https://github.com/PacificBiosciences/kineticsTools/blob/master/doc/manual.rst (2018) ("kineticsTools manual")
1022	Liu et al., "Detection of DNA Base Modifications by Deep Recurrent Neural Network on Oxford Nanopore Sequencing Data," Nature Comms. 10(1) (Jun. 4, 2019) ("Q. Liu")
1023	Eid et al., "Real-time DNA sequencing from single polymerase molecules," Science 323(5910) (2009)
1024	Int. Appl. Publ. No. WO 2012/065043 ("Flusberg PCT")
1025	Jonas Korf & Stephen W. Turner, "Single-Molecule Sequencing" in Encyclopedia of Biophysics (2013) ("Korf")
1026	GenomeWeb, "PacBio Reveals Beta System Specs for RS; Says Commercial Release is on Track for First Half of 2011," https://www.genomeweb.com/sequencing/pacbios-q3-losses-widen-itreadies-launch-rs-system (2010) ("GenomeWeb")
1027	Jacob Schreiber et al., "Error Rates for Nanopore Discrimination among Cytosine, Methylcytosine, and Hydroxymethylcytosine along Individual DNA Strands," Proceedings of the National Academy of Sciences 110(47) (2013) ("Schreiber")
1028	Langlotz, A Roadmap for Foundational Research on Artificial Intelligence in Medical Imaging: From the 2018 NIH/RSNA/ACR/The Academy Workshop, Radiology 291(3) (Apr. 16, 2019) ("Langlotz")
1029	Miotto et al., "Deep Learning for Healthcare: Review, Opportunities and Challenges," Briefings in Bioinformatics, 19(6) (2018) ("Miotto")

Petitioner's Exhibits	
No.	Description
1030	Tse et al., "Genome-wide Detection of Cytosine Methylation by Single Molecule Real-time Sequencing," Proceedings of the National Academy of Sciences, 118(5) (2021) ("Tse")
1031	Tiernan Ray, "AI is Changing the Entire Nature of Compute," ZDNet, http://web.archive.org/web/20190630155704/https://www.zdnet.com/article/ai-is-changing-the-entire-nature-of-compute/ (June 30, 2019) ("Ray")
1032	Wenger et al., "Accurate Circular Consensus Long-read Sequencing Improves Variant Detection and Assembly of a Human Genome," Nature Biotechnology, 37(10) (Aug. 12, 2019) ("Wenger")
1033	Pacific Biosciences, PacBioFileFormats Documentation (Feb. 2022) ("PacBioFileFormats-2022")
1034	Lau et al., "LongISLND: in silico Sequencing of Lengthy and Noisy Datatypes," Bioinformatics, 32(24) (2016) ("Lau")
1035	Tahir et al., "iRNA-PseKNC(2methyl): Identify RNA 2'-O-methylation Sites by Convolution Neural Network and Chou's Pseudo Components," Journal of Theoretical Biology, 465 (2018) ("Tahir")
1036	DeepVariant Usage Guide, https://github.com/google/deepvariant/blob/42b9c777436d8306f6cb9d2e18da756fa370fcd8/docs/deepvariant-details.md ("DeepVariant")
1037	U.S. Patent Application No. 18/189,084 File History
1038	Liu et al., "Accurate Detection of m6A RNA Modifications in Native RNA Sequences," https://www.biorxiv.org/content/10.1101/525741v1 (Jan. 21, 2019) ("H. Liu")
1039	First Declaration of Nathaniel E. Frank-White
1040	Second Declaration of Nathaniel E. Frank-White

Petitioner's Exhibits	
No.	Description
1041	Declaration of Mozhgan Novbakhtian
1042	GitHub, PacBio BAM 3.0, https://github.com/PacificBiosciences/PacBioFileFormats/blob/3.0/BAM.rst (Jan 25, 2017)
1043	GitHub, PacBio BAM 5.0, https://github.com/PacificBiosciences/PacBioFileFormats/blob/5.0/BAM.rst (Jan 25, 2017)
1044	PacBio Sequencing – How it Works video file
1045	U.S. Patent No. 11,844,666 to Flusberg et al. (“Flusberg-666”)
1046	U.S. Patent Application No. 17/891,899 File History
1047	DNA Modification Detection with SMRT® Sequencing Using R (November 15, 2011)
1048	Pacific Biosciences Press Release – New Sequel II System, Featuring ~8 Times the DNA Sequencing Data Output, https://www.pacb.com/press_releases/pacific-biosciences-launchesnew-sequel-ii-system-featuring-8-times-the-dna-sequencing-dataoutput/ (April 24, 2019)
1049	Deposition Transcript of Dr. Peter Koo
1050	Petitioner's Demonstratives

Patent Owner's Exhibits	
No.	Description
2001	Color Drawings of US 11,091,794 Downloaded from USPTO Patent Center
2002	Declaration of Dr. Peter Koo
2003	Dr. Peter Koo's CV
2004	Li et al. and 1000 Genome Project Data Processing Subgroup. 2009. "The Sequence Alignment/Map format and SAMtools," <i>Bioinformatics</i> 25(16): 2078-2079 ("Li")
2005	Suzuki et al., "AgIn: measuring the landscape of CpG methylation of individual repetitive elements," <i>Bioinformatics</i> , 32(19), 2016, 2911–2919 ("Suzuki")
2006	Zheng and Casari, "Feature Engineering for Machine Learning," First Edition, O'Reilly Media, Inc., Sebastopol, CA, 2018 (Excerpts)
2007	Web page (print friendly screen capture): Johns Hopkins University Center for Computational Biology, StringTie – Transcript assembly and quantification for RNA-Seq. URL: http://ccb.jhu.edu/software/stringtie/index.shtml . Web page visited January 23, 2024
2008	Web page (print friendly screen capture): Broad Institute Genome Analysis Toolkit. URL: http://gatk.broadinstitute.org/hc/en-us . Web page visited January 23, 2024
2009	Web page (print friendly screen capture): Broad Institute Genome Analysis Toolkit - HaplotypeCaller. March 4, 2020. URL: http://gatk.broadinstitute.org/hc/en-us/articles/360040096812-HaplotypeCaller . Web page visited January 23, 2024

Patent Owner's Exhibits	
No.	Description
2010	Web page: University of California at Santa Cruz, Genome Browser BAM Track Format. URL: https://genome.ucsc.edu/goldenPath/help/bam.html . Web page visited January 23, 2024
2011	Web page (print friendly screen capture): Git Hub HPC Training – Peak calling with MACS2. June 12, 2017. URL: https://hbctraining.github.io/Intro-to-ChIPseq/lessons/05_peak_calling_mac2.html . Web page visited January 23, 2024
2012	YouTube Video: PacBio Data Deep Dive: A Closer Look at HiFi Sequencing. PacBio May 24, 2021. URL: https://www.youtube.com/watch?v=1aqnLQ-nwYk . Downloaded January 22, 2024. (Also available at https://www.pacb.com/videos/pacbio-data-deep-dive-a-closer-look-at-hifi-sequencing/)
2013	Screen Capture of Exhibit 2012 (YouTube) https://www.youtube.com/watch?v=1aqnLQ-nwYk
2014	Screen Capture of Exhibit 2012 (PacBio.com) https://www.pacb.com/videos/pacbio-data-deep-dive-a-closer-look-at-hifi-sequencing/
2015	Transcript of 9:50 – 11:45 of Exhibit 2012
2016	<i>Take2 Technologies Limited v. Pacific Biosciences of California, Inc.</i> , U.S. District Court for the District of Delaware, Case No. 5:23-cv-04166-EJD, Dkt. 8, Complaint (Public Redacted Version), December 14, 2022

Patent Owner's Exhibits	
No.	Description
2017	<i>Take2 Technologies Limited v. Pacific Biosciences of California, Inc.</i> , 5:23-cv-04166-EJD, Dkt. 8-2, Exhibit C to the Complaint – Transcript of PacBio Q4 2020 Earnings call on February 10, 2021 (available at https://www.fool.com/earnings/call-transcripts/2021/02/10/pacific-biosciences-of-californiapacb-q4-2020-ear/) (Complaint Ex. C)
2018	<i>Take2 Technologies Limited v. Pacific Biosciences of California, Inc.</i> , 5:23-cv-04166-EJD, Dkt. 8-2, Exhibit E to the Complaint – PacBio Children's Mercy Kansas City Press Release dated April 21, 2022 (available at https://www.pacb.com/press_releases/pacbio-and-childrens-mercy-kansas-city-expand-collaboration-taking-a-multi-omics-approach-to-characterize-rare-disease/) (Complaint Ex. E)
2019	<i>Take2 Technologies Limited v. Pacific Biosciences of California, Inc.</i> , 5:23-cv-04166-EJD, Dkt. 8-2, Exhibit F to the Complaint - Screenshot PacBio Products - Epigenetics (available at https://www.pacb.com/products-and-services/applications/epigenetics/) (Complaint Ex. F)
2020	YouTube Video: "HiFi Sequencing: See What You've Been Missing." PacBio, November 2, 2021. URL: https://www.youtube.com/watch?v=d2an7LXhPSU . Downloaded January 19, 2024. (Also available at https://www.pacb.com/videos/hifi-sequencing-see-what-youve-been-missing/)
2021	Screen Capture of Exhibit 2020 (YouTube) https://www.youtube.com/watch?v=d2an7LXhPSU
2022	Screen Capture of Exhibit 2020 (PacBio.com) https://www.pacb.com/videos/hifi-sequencing-see-what-youve-been-missing/
2023	Transcript of 05:05-06:06 from Exhibit 2020

Patent Owner's Exhibits	
No.	Description
2024	YouTube Video: "Methylation Detection with PacBio HiFi Sequencing: ASHG 2021." PacBio, October 27, 2021. URL: https://www.youtube.com/watch?v=rT231BCp6Ro . Downloaded January 17, 2024.
2025	Screen Capture of Exhibit 2024 (YouTube) https://www.youtube.com/watch?v=rT231BCp6Ro
2026	Transcript of 15:46–15:56 from Exhibit 2024
2027	Web page: PacBio Sequencing 101: The SMRT Cell in PacBio long-read sequencing. URL: https://www.pacb.com/blog/smrt-cell/ . Web page visited January 23, 2024
2028	<i>Take2 Technologies Limited v. Pacific Biosciences of California, Inc.</i> , 5:23-cv-04166-EJD, Dkt. 8-2, Exhibit D to the Complaint – PacBio SMRT® Link release notes (v11.0) (Complaint Ex. D)
2029	U.S. Patent Application Publication US2010/0221716 by Flusberg
2030	Declaration of Amy Candeloro, January 26, 2024
2031	Declaration of Chelsea Baker
2032	List of Materials Considered by Dr. Peter K. Koo
2033	Patent Owner's Notice of Deposition of Dr. Christophe Dessimoz, June 7, 2024
2034	Patent Owner's Notice of Deposition of Mozghan Novbakhtian, June 7, 2024
2035	Document entitled "MEASURING DNA METHYLATION WITH 5-BASE HIFI 16 SEQUENCING"
2036	LinkedIn Profile for Mozghan Novbakhtian

Patent Owner's Exhibits	
No.	Description
2037	Transcript of Deposition of Christophe Dessimoz, Ph.D., June 21, 2024
2038	Beaulaurier et al., “Deciphering bacterial epigenomes using modern sequencing technologies,” <i>Nat Rev Genet</i> 20, 157–172 (2019) (“Beaulaurier”)
2039	Birknerova et al., “Circulating Cell-Free DNA-Based Methylation Pattern in Saliva for Early Diagnosis of Head and Neck Cancer,” <i>Cancers</i> , 14, 4882 (2022) (“Birknerova”)
2040	Gouil et al., “Latest techniques to study DNA methylation,” <i>Essays in Biochemistry</i> , 63, 639–648 (2019) (“Gouil”)
2041	Supplemental Declaration of Dr. Peter K. Koo
2042	Sang, “Bioinformatics Analysis of DNA Methylation Through Bisulfite Sequencing Data,” <i>Methods Mol. Biol.</i> , 2198:441-450 (2021) (“Sang”)
2043	Wang et al., “Factors and Methods for the Detection of Gene Expression Regulation,” <i>Biomolecules</i> , 13, 304 (2023) (“Wang”)
2044	Cheung et al., “Direct haplotype-resolved 5-base HiFi sequencing for genome-wide profiling of hypermethylation outliers in a rare disease cohort,” <i>Nature Communications</i> , 14, 3090 (2023) (“Cheung”)
2045	Web page: Oxford Nanopore Technologies – How nanopore sequencing works. URL: https://nanoporetech.com/platform/technology . Web page visited July 25, 2024.
2046	Web page: Your Genome – What is Oxford Nanopore Technology (ONT) sequencing? URL: https://www.yourgenome.org/theme/what-is-oxford-nanopore-technology-ont-sequencing/ . Web page visited July 25, 2024.

Patent Owner's Exhibits	
No.	Description
2047	PDF downloaded from web page: Genome-wide CpG methylation calling with standard HiFi shole genome sequencing ("PacBio's Primrose Poster"). URL: https://www.pacb.com/wp-content/uploads/ESHG-2022-Genome-wide-CpG-methylation-calling-Blethrow-Poster.pdf . Web page visited July 25, 2024.
2048	Web page: ESHG Conference 2022. https://2022.eshg.org/ Web page visited July 25, 2024.
2049	Web page: ESHG 2022 Sequence Without Compromise PacBio. URL: https://programs.pacificbiosciences.com/l/1652/2022-03-17/43c8ch . Web page visited July 25, 2024.
2050	Searle et al., "Third-Generation Sequencing of Epigenetic DNA," <i>Angew. Chem. Int. Ed.</i> 62, e202215704 (2023) ("Searle")
2051	Gigante et al., "Using long-read sequencing to detect imprinted DNA methylation," <i>Nucleic Acids Research</i> , 47(8), e46 (2019) ("Gigante")
2052	CV of Dr. Peter K. Koo, updated July 26, 2024
2053	Web page: PacBio Transforms Access to the Epigenome and Streamlines Workflows, PacBio press release dated April 21, 2022. URL: https://www.pacb.com/press_releases/pacbio-transforms-access-to-the-epigenome-and-streamlines-workflows/ . Web page visited July 26, 2024.
2054	Comparison of '794 patent claim 1, EX1030, EX2024, and EX2047
2055	Additional list of Materials Considered by Dr. Peter K. Koo for preparation of Supplemental Declaration of Dr. Peter K. Koo (EX2041)
2056	Declaration of Amy Candeloro, July 26, 2024
2057	Declaration of Amy Candeloro, August 14, 2024 (Supplemental Evidence – Served Only)

Patent Owner's Exhibits	
No.	Description
2058	Web page returned at the following URL: https://github.com/PacificBiosciences/R-kinetics , last accessed January 15, 2025
2059	Web page returned at the following URL: https://www.pacb.com/press_releases/pacific-biosciences-launches-new-sequel-ii-system-featuring-8-times-the-dna-sequencing-data-output/ , last accessed January 15, 2025
2060	Declaration of Amy Candeloro, January 16, 2025
2061	CONFIDENTIAL - PacBio – CUHK Assignment and Settlement Agreement.
2062	CONFIDENTIAL - PacBio – Take2 Mutual Release

Respectfully submitted,

Date: March 20, 2025

By: / Michael J. Wise /
Michael J. Wise, Reg. No. 34,047
Perkins Coie LLP
1888 Century Park East, Suite 1700
Los Angeles, CA 90067
Phone: 310-788-3271
Counsel for Patent Owner

CERTIFICATE OF SERVICE

The undersigned hereby certifies that service on Petitioner was made as follows, in accordance with 37 C.F.R. § 42.6(e):

Date of service: Mach 20, 2025

Manner of service: 1. Electronic submission through the USPTO Patent Trial and Appeal Board P-TACTS System
2. Electronic mail

Document(s) served: **SUBMISSION OF EXHIBITS 2061 AND 2062 AND
UPDATED EXHIBIT LIST**

Persons served: Michael T. Rosato (Reg. No. 52,182)
mrosato@wsgr.com

Sonja R. Gerrard (Reg. No. 72,802)
sgerrard@wsgr.com

Patrick M. Medley (Reg. No. 74,735)
pmedley@wsgr.com

/ Amy Candeloro /

Paralegal
Perkins Coie LLP