

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BRUKER SPATIAL BIOLOGY, INC.,
Petitioner

v.

PRESIDENT AND FELLOWS OF HARVARD COLLEGE and 10X GENOMICS,
INC.,
Patent Owner

Case IPR2024-00526
U.S. Patent No. 11,542,554

**PATENT OWNER'S RESPONSE TO PETITIONER'S
MOTION TO SEAL EXHIBIT 1083**

Mail Stop "PATENT BOARD"
Patent Trial and Appeal Board
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	GOVERNING RULES AND PTAB GUIDANCE.....	1
III.	GOOD CAUSE EXISTS FOR SEALING EXHIBIT 1083	2
IV.	A REDACTED VERSION OF EX1083 IS PROVIDED	5
V.	DEFAULT PROTECTIVE ORDER.....	5
VI.	CERTIFICATION OF NONPUBLICATION	5
VII.	CONCLUSION	5

PATENT OWNER'S UPDATED EXHIBIT LIST

Exhibit No.	Description
2001	Stahl <i>et al.</i> , “Visualization and analysis of gene expression in tissue selections by spatial transcriptomics,” <i>Science</i> 353(6294):78-82 (July 1, 2016), with attached Supplementary Materials
2002	<i>Withdrawn</i>
2003	International Patent Application Publication No. WO 2012/140224 A1 to Frisen <i>et al.</i> , published October 18, 2012
2004	“No-Heat Flow Cell (FSC2),” Biopetechs Inc., accessible at https://biopetechs.com/product/no-heat-flow-cell-fcs2/ (last accessed May 24, 2024)
2005	“FCS2 Chamber,” Biopetechs Inc., accessible at https://biopetechs.com/product/fcs2-chamber/ (last accessed May 24, 2024)
2006	Prosecution File History of U.S. Patent No. 11,542,554
2007	Fang, <i>et al.</i> , “Three-dimensional single-cell transcriptome imaging of thick tissues,” <i>eLife</i> , August 16, 2023, accessible at https://elifesciences.org/reviewed-preprints/90029 (last accessed May 23, 2024) (“Zhuang 2023”)
2008	Lu, <i>et al.</i> , “Spatially resolved epigenomic profiling of single cells in complex tissues,” <i>Cell</i> 185:4448–4464 (2022)
2009	Su, <i>et al.</i> , “Genome-Scale Imaging of the 3D Organization and Transcriptional Activity of Chromatin,” <i>Cell</i> 182:1641–1659 (2020)
2010	Cox, Jr., <i>et al.</i> , “Organizing your space: The potential for integrating spatial transcriptomics and 3D imaging data in plants,” <i>Plant Physiology</i> 188:703-712 (2022) (“Czymmek 2022”)

Exhibit No.	Description
2011	Ghani, <i>et al.</i> , “Optimisation of MERFISH Data Analysis and Visualisation,” May 21, 2019, accessible at https://www.ucl.ac.uk/~ucbpngh/MiniProject3.pdf (last accessed May 28, 2024)
2012	<i>Withdrawn</i>
2013	Docket Report, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), July 8, 2024
2014	Oral Order, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 109, April 25, 2023
2015	Hearing Transcript, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), June 14, 2024
2016	Notice of Service of 10x Genomics, Inc.’s Initial Infringement Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 68, November 23, 2022
2017	Notice of Service of NanoString Technologies, Inc.’s Initial Invalidity Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 79, January 3, 2023
2018	Notice of Service of 10x Genomics, Inc.’s Supplemental Infringement Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 100, March 24, 2023
2019	Notice of Service of NanoString Technologies, Inc.’s Supplemental Invalidity Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 132, May 17, 2023
2020	Memorandum Opinion and Order, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 269, February 1, 2024

Exhibit No.	Description
2021	Notice of Service of NanoString Technologies, Inc.’s Initial Infringement Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 64, November 23, 2022
2022	Notice of Service of 10x Genomics, Inc.’s Initial Invalidity Contentions, <i>10x Genomics, Inc. v. NanoString Techs., Inc.</i> , Case No. 1:22-cv-00261 (D. Del.), ECF No. 77, December 27, 2022
2023	E-mail Correspondence from Jason J. Rawnsley to Melissa Astell, July 8, 2024
2024	Declaration of Hari Shroff, Ph.D., in Support of Patent Owner’s Response
2025	<i>Curriculum Vitae</i> of Hari Shroff, Ph.D.
2026	Declaration of Julie L. Davis in Support of Patent Owner’s Response
2027	<i>Curriculum Vitae</i> of Julie L. Davis
2028	“Bruker Completes Asset Acquisition of NanoString Business,” Bruker Corporation Press Release, May 6, 2024 (accessible at https://ir.bruker.com/press-releases/press-release-details/2024/Bruker-Completes-Asset-Acquisition-of-NanoString-Business/default.aspx , last accessed December 9, 2024)
2029	“Who We Are,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/about-us/ , last accessed December 9, 2024)
2030	“CosMx™ SMI for Single-Cell Imaging,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/products/cosmx-spatial-molecular-imager/single-cell-imaging-overview/ , last accessed December 9, 2024)

Exhibit No.	Description
2031	“NanoString Begins Commercial Shipments of CosMx Spatial Molecular Imager and AtoMx Spatial Informatics Platform,” BusinessWire, December 6, 2022 (accessible at https://www.businesswire.com/news/home/20221206005433/en/NanoString-Begins-Commercial-Shipments-of-CosMx-Spatial-Molecular-Imager-and-AtoMx-Spatial-Informatics-Platform , last accessed December 9, 2024)
2032	NanoString Technologies, Inc. Form 10-K for the fiscal year ended December 31, 2022
2033	“Our mission,” 10x Genomics, Inc. (accessible at https://www.10xgenomics.com/company , last accessed December 9, 2024)
2034	10x Genomics, Inc. Form 10-K for the fiscal year ended December 31, 2023
2035	“10x Genomics Commercially Launches Xenium Platform for In Situ Analysis,” PR Newswire, December 8, 2022 (accessible at https://www.prnewswire.com/news-releases/10x-genomics-commercially-launches-xenium-platform-for-in-situ-analysis-301698748.html , last accessed December 9, 2024)
2036	“Xenium In Situ,” 10x Genomics, Inc. (accessible at https://www.10xgenomics.com/platforms/xenium , last accessed December 9, 2024)
2037	“10x Genomics Begins Commercial Shipments of Xenium Prime 5K Pan-Tissue and Pathways Panel,” PR Newswire, June 20, 2024 (accessible at https://www.prnewswire.com/news-releases/10x-genomics-begins-commercial-shipments-of-xenium-prime-5k-pan-tissue-and-pathways-panel-302177116.html , last accessed December 9, 2024)

Exhibit No.	Description
2038	“The First Fully Integrated Single-Cell Spatial Solution,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/products/atomx-spatial-informatics-platform/cosmx-and-atomx-the-first-fully-integrated-single-cell-spatial-solution/ , last accessed December 9, 2024)
2039	“CosMx™ SMI Technology Access Program,” NanoString Technologies, Inc. (accessible at https://nanosttring.com/products/cosmx-spatial-molecular-imager/technology-access-program/ , last accessed December 9, 2024)
2040	“Accelerating the Mastery of Biology to Advance Human Health,” 42 nd Annual J.P. Morgan Healthcare Conference, dated 2024 (accessible at https://s28.q4cdn.com/592666581/files/doc_presentations/2024/01/2024-TXG-JPM-Healthcare-Presentation-vF.pdf , last accessed December 9, 2024)
2041	Chen, K. H., “Spatially resolved, highly multiplexed RNA profiling in single cells,” Dissertation, Harvard University, April 2015
2042	Uchida, A., et al., “Live-cell imaging of neurofilament transport in cultured neurons,” <i>Methods Cell Biol.</i> , 131:21-90 (2016)
2043	Transcript of the Deposition of Kirk Czymmek, Ph.D.
2044	Zhang, B., “Gaussian approximations of fluorescence microscope point-spread function models,” <i>Applied Optics</i> , 46(10):1819-1829 (April 1, 2007)
2045	Waters, J., “Accuracy and precision in quantitative fluorescence microscopy,” <i>The Journal of Cell Biology</i> 185(7):1135-1148 (2009)
2046	Conchello, J., et al., “Optical sectioning microscopy,” <i>Nature Methods</i> , 2(12):920-931

Exhibit No.	Description
2047	Stallinga, S., et al., “Accuracy of the Gaussian Point Spread Function model in 2D localization microscopy,” <i>Optics Express</i> , 18(24):24461-22476 (November 22, 2010)
2048	McCall, B., “FLUORESCENCE MICROSCOPY/QUANTITATIVE IMAGING: A systems-engineering approach to quantitative fluorescence bioimaging,” laserfocusworld.com, January 21, 2015 (accessible at https://www.laserfocusworld.com/biooptics/bioimaging/fluorescence/article/14190740/fluorescence-microscopy-quantitative-imaging-a-systems-engineering-approach-to-quantitative-fluorescence-bioimaging , last accessed December 9, 2024)
2049	Davis, A., et al., “Characterizing and Diminishing Autofluorescence in Formalin-fixed Paraffin-embedded Human Respiratory Tissue,” <i>Journal of Histochemistry & Cytochemistry</i> , 62(6):405-423 (2014)
2050	Lee, J., et al., “Highly Multiplexed Subcellular RNA Sequencing in Situ,” <i>Science Reports</i> , 343:1360-1363 (March 21, 2014), with supplemental materials
2051	Lubeck, E., et al., “Single cell systems biology by super-resolution imaging and combinatorial labeling,” <i>Nature Methods</i> , 9(7):743-748 (June 2012), with supplemental materials
2052	Lubeck, E., et al., “Single-cell in situ RNA profiling by sequential hybridization,” <i>Nature Methods</i> , 11(4):360-361 (April 2014)
2053	Moffitt, J., et al., “High-throughput single-cell gene-expression profiling with multiplexed error-robust fluorescence in situ hybridization,” <i>PNAS</i> , 113(39):11046-11051 (September 27, 2016)
2054	Response to Office Action, U.S. Patent Application No. 17/374,000, filed January 26, 2024
2055	Response to Office Action, U.S. Patent Application No. 18/184,967, filed November 22, 2023

Exhibit No.	Description
2056	<i>Intentionally Left Blank</i>
2057	U.S. Patent Application Publication No. 2012/0040397 A1 to Luo et al., published February 16, 2012
2058	U.S. Patent Application Publication No. 2014/0220587 A1 to Green, Jr. et al., published August 7, 2014
2059	Chung, K., et al., “CLARITY for mapping the nervous system,” <i>Nature Methods</i> , 10(6):508-513 (2013)
2060	Xenium Analyzer User Guide, CG000584, Rev. G., 10x Genomics, Inc.
2061	CosMx® SMI Manual, MAN-10161-08, Software v1.4.1, Bruker Spatial Biology, Inc.
2062	Manual Slide Preparation, CosMX™ Spatial Molecular Imager, MAN-10159-01, NanoString Technologies, Inc.
2063	<i>Intentionally Left Blank</i>
2064	Cassini HW.V1 Design Review and Transfer to NPI, June 1, 2022, 10XH-00054907-96 (CONFIDENTIAL – PROTECTIVE ORDER MATERIAL)
2065	CosMx™ Spatial Molecular Imager Grant Support Document, NanoString Technologies, Inc.
2066	<i>Intentionally Left Blank</i>
2067	<i>Intentionally Left Blank</i>
2068	<i>Intentionally Left Blank</i>
2069	<i>Intentionally Left Blank</i>
2070	“New Insights Into Cleft Palate Unlocked With 10x Genomics’ Single Cell and Spatial Technologies,” 10x Genomics, Inc. Press Release, June 27, 2024

Exhibit No.	Description
2071	“10x Genomics Surpasses 100 Xenium Analyzer Shipments,” BioSpace, August 29, 2023 (accessible at https://www.biospace.com/10x-genomics-surpasses-100-xenium-analyzer-shipments , last accessed November 24, 2024)
2072	Peroni, E., “Spatial-transcriptomic profiling: a new lens for understanding myelofibrosis pathophysiology,” <i>Cell Communication and Signaling</i> , 22:510 (2024)
2073	Cassini Phase 2 Design Review – Instrument and Software, July 13, 2022, 10X261-00003121-232 (CONFIDENTIAL – PROTECTIVE ORDER MATERIAL)
2074	Small, A., et al., “Fluorophore localization algorithms for super-resolution microscopy,” <i>Nature Methods</i> , 11(3):267-279 (March 2014)
2075	Huang, F., et al., “Simultaneous multiple-emitter fitting for single molecule super-resolution imaging,” <i>Biomedical Optics Express</i> , 2(5):1377-1393 (May 1, 2011)
2076	Dobrucki, J., et al., “Scattering of Exciting Light by Live Cells in Fluorescence Confocal Imaging: Phototoxic Effects and Relevance for FRAP Studies,” <i>Biophysical Journal</i> , 93:1778-1786 (September 2007)
2077	Booth, M., “Adaptive optical microscopy: the ongoing quest for a perfect image,” <i>Light: Science & Applications</i> , 3, e165 (2014)
2078	Diaspro, A., et al., “Optical nanoscopy,” <i>La Rivista del Nuovo Cimento</i> , 43:385-455 (2020)
2079	Lee, J., et al., “Fluorescent <i>in situ</i> sequencing (FISSEQ) of RNA for gene expression profiling in intact cells and tissues,” <i>Nature Protocols</i> , 10(3):442-458 (2015)
2080	Schoder, D., et al., “Novel Approach for Assessing Performance of PCR Cyclers Used for Diagnostic Testing,” <i>Journal of Clinical Microbiology</i> , 43(6):2724-2728 (June 2005)

Exhibit No.	Description
2081	Ettinger, A., et al., “Fluorescence Live Cell Imaging,” <i>Methods Cell Biol.</i> , 123:77-94 (2014)
2082	<i>Intentionally Left Blank</i>
2083	Public Redacted Version of Exhibit 1083 (“Transcript of the Deposition of Julie Davis”)

I. INTRODUCTION

Pursuant to 37 C.F.R. § 42.25(a), Patent Owner (Exclusive Licensee) 10x Genomics, Inc. (“10x”) submits this response to Petitioner’s Motion to Seal Exhibit 1083 (Paper 28). This response is timely filed within one month from the date of service of Petitioner’s Motion to Seal Exhibit 1083. 37 C.F.R. § 42.25(a)(1). Good cause exists to seal Exhibit 1083 because it includes 10x’s highly confidential, competitively sensitive information. 10x reiterates its request for entry of the Default Protective Order. *See* Paper 22, Patent Owner’s Motion to Seal, at 1, 7. Petitioner has stated that it does not oppose 10x’s request to seal Exhibit 1083. Paper 28, 2, 4.

II. GOVERNING RULES AND PTAB GUIDANCE

“A party intending a document or thing to be sealed shall file a motion to seal concurrent with the filing of the document or thing to be sealed. The document or thing shall be provisionally sealed on receipt of the motion and remain so pending the outcome of the decision on the motion.” 37 C.F.R. § 42.14. The Consolidated Trial Practice Guide (“TPG”) explains that “the rules aim to strike a balance between the public’s interest in maintaining a complete and understandable file history and the parties’ interest in protecting truly sensitive information.” TPG at 19. As the TPG states, “[t]he rules identify confidential information in a manner consistent with Federal Rule of Civil Procedure

26(c)(1)(G), which provides for protective orders for trade secret or other confidential research, development, or commercial information.” *Id.* (citing 37 C.F.R. § 42.54).

In determining whether to grant a Motion to Seal, the Board must find “good cause.” 37 C.F.R. § 42.54(a). Good cause for sealing material can be established by demonstrating that the balance of the following considerations favors sealing the material: whether (1) the information sought to be sealed is truly confidential, (2) a concrete harm would result upon public disclosure, (3) there exists a genuine need to rely in the trial on the specific information sought to be sealed, and (4), on balance, an interest in maintaining confidentiality outweighs the strong public interest in having an open record. *See Argentum Pharms. LLC v. Alcon Research, Ltd.*, IPR2017-01053, Paper 27 at 4 (P.T.A.B. Jan. 19, 2018) (informative).

III. GOOD CAUSE EXISTS FOR SEALING EXHIBIT 1083

Exhibit 1083 is the deposition transcript of 10x’s economics expert, Ms. Julie Davis. Exhibit 1083 contains confidential financial information pertaining to sales revenue associated with 10x’s Xenium product. Ms. Davis initially provided opinions on the commercial success of the Xenium product in her declaration (EX2026), in which she relied upon proprietary financial information belonging to 10x and disclosed in Appendixes B and C of her declaration. *See* EX2026, ¶¶33-35, Appendix B, Appendix C. 10x accordingly has already filed an unopposed

motion to seal Ms. Davis' declaration, and has filed a public, redacted version of EX2026. *See* Paper 22 at 4-6; EX2026 (redacted).

Good cause exists to seal EX1083 for the same reasons 10x provided for sealing EX2026. During deposition, Ms. Davis was asked questions involving the same proprietary financial information discussed in Ms. Davis' declaration EX2026. Accordingly, counsel for 10x timely designated EX1083 as confidential, and Petitioner filed EX1083 under seal. *See* EX2083 (public, redacted version of EX1083), 125:5-12. To the best of the Undersigned's knowledge, the confidential information in EX1083 has not been published or otherwise made public, and 10x has undertaken efforts to maintain the confidentiality of this information in the parallel district court litigation. Exhibit 1083 is marked as "CONFIDENTIAL-SUBJECT TO PROTECTIVE ORDER."

Exhibit 1083 contains "commercial information" under 37 C.F.R. § 42.54(a)(7). The Board's Default Protective Order permits for protection of sensitive commercial information. *See* TPG at 19 (defining "confidential information" to match Fed. R. Civ. P. 26(c)(1)(G), including "other . . . commercial information"). The Board consistently seals product sales and internal financial documents. *See, e.g., Echelon Fitness Multimedia, LLC v. Peleton Interactive, Inc.*, IPR2020-01541, Paper 54, at 87-89 (P.T.A.B. Mar. 2, 2022); *Quest USA Corp. v. PopSockets LLC*, IPR2018-00497, Paper 59 at 87-90

(P.T.A.B. Aug. 12, 2019); *Arista Networks, Inc. v. Cisco Sys., Inc.*, IPR2016-00309, Paper 51 at 2-3 (P.T.A.B. May 8, 2017). Accordingly, EX1083 should be subject to the protection of the Board's Default Protective Order.

10x would suffer concrete harm from the public disclosure of EX1083. The confidential financial information therein could provide competitor insight into 10x's pricing and marketing decisions. Such competitor insight could motivate copying and infringement of 10x's intellectual property.

Petitioner relies on EX1083 in this proceeding. *See e.g.*, Paper 27 at 22. The confidential information EX1083 is pertinent to objective indicia of commercial success of 10x's Xenium product. This confidential information is not available from any non-confidential sources.

The interest in maintaining confidentiality outweighs the public interest in having an open record. Exhibit 1083 contains financial information of 10x's Xenium product, and if publicly disclosed, 10x risks significant competitive harm. In contrast, sealing of EX1083 deprives the public of only the confidential information related to 10x's pricing and marketing decisions for the Xenium product. Furthermore, the public's interest in an open record is served as the general facts on commercial success of the Xenium product are provided in the papers and public exhibits, including the public, redacted version of EX1083, contemporaneously filed herewith.

Accordingly, 10x respectfully requests that the Board grant Petitioner's Motion to Seal EX1083. Paper 28.

IV. A REDACTED VERSION OF EX1083 IS PROVIDED

In an effort to balance “the public’s interest in maintaining a complete and understandable file history,” 10x has concurrently filed a public version of EX1083 (*see* EX2083), with redactions of the confidential information. TPG at 19.

V. DEFAULT PROTECTIVE ORDER

10x submits that the confidential information referenced herein be subject to the Board’s Default Protective Order, previously submitted as Exhibit A with Patent Owner’s Motion to Seal. *See* Paper 22, Exhibit A; 37 C.F.R. § 42.54(a).

VI. CERTIFICATION OF NONPUBLICATION

Undersigned counsel certifies that the information sought to be sealed has not, to their knowledge, been published or otherwise made public.

VII. CONCLUSION

For the foregoing reasons, 10x respectfully requests that the Board enter Default Protective Order and grant Petitioner’s Motion to Seal EX1083. Paper 28.

Respectfully submitted,

STERNE KESSLER GOLDSTEIN & FOX PLLC

/David H. Holman/

David H. Holman, Ph.D.
Registration No. 61,205
Lead Attorney for Exclusive Licensee

Date: April 18, 2025

1101 K Street, NW, 10th Floor
Washington, DC 20005
(202) 371-2600

CERTIFICATION OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PATENT OWNER'S RESPONSE TO PETITIONER'S MOTION TO SEAL EXHIBIT 1083** and **EXHIBIT 2083** were served in their entireties on April 18, 2025, upon the following parties via email:

Counsel for Petitioner Bruker Spatial Biology, Inc.

Derek C. Walter (Lead Counsel)
Concord Cheung (Back-up Counsel)
WEIL, GOTSCHAL & MANGES LLP
dwalter@jonesday.com
concordcheung@jonesday.com
EXT-Bruker-10x@groups.jonesday.com

Counsel for Patent Owner President and Fellows of Harvard College

Ruben J. Rodrigues (Lead Counsel)
Sarah E. Rieger (Back-up Counsel)
FOLEY & LARDNER LLP
rrodrigues@foley.com
srieger@foley.com
BOST-F-10Xv.Nanostring@foley.com

Respectfully submitted,

STERNE KESSLER GOLDSTEIN & FOX PLLC

/David H. Holman/

David H. Holman, Ph.D.
Registration No. 61,205
Lead Attorney for Exclusive Licensee

Date: April 18, 2025

1101 K Street, NW, 10th Floor
Washington, DC 20005
(202) 371-2600