IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BECTON, DICKINSON AND COMPANY and CELLULAR RESEARCH, INC.,	)	
Plaintiffs,	)	
	)	C.A. No. _____
v.	)	
	)	**DEMAND FOR JURY TRIAL**
10X GENOMICS, INC.,	)	
Defendant.	)	

COMPLAINT

Becton, Dickinson and Company ("BD") and Cellular Research, Inc. ("Cellular Research" and collectively with BD, "Plaintiffs") hereby allege for their Complaint against Defendant 10X Genomics, Inc. ("10X," or "Defendant"), as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the United States Patent Act, 35 U.S.C. §§1 *et seq.,* including 35 U.S.C. § 271.

2. BD and Cellular Research bring this action to seek relief for 10X's infringement of Plaintiffs' rights arising under the Patent Laws of the United States 35 U.S.C. §1, *et. seq.,* from U.S. Patent Nos. 8,835,358, 9,845,502, 9,315,857, 9,816,137, 9,708,659, 9,290,808, and 9,290,809 (collectively the "Fodor patents"), and from U.S. Patent Nos. 9,567,645, 9,567,646, 9,598,736, and 9,637,799 (collectively the "Fan patents" and collectively with the Fodor patents, "the Asserted Patents").

THE PARTIES

3. BD is a corporation organized and existing under the laws of New Jersey, with its principal place of business at 1 Becton Drive, Franklin Lakes, NY 07417. BD is the current owner by assignment of each of the Fodor and Fan patents.

4. Cellular Research is a corporation organized and existing under the laws of Delaware, with its principal place of business at 4040 Campbell Avenue, Suite 110, Menlo Park, CA 94025. Cellular Research was the previous owner by assignment of each of the Fodor and Fan patents.

5. Upon information and belief, 10X is a company organized and existing under the laws of Delaware, with its principal place of business at 7068 Koll Center Parkway, Suite 401, Pleasanton, CA, 94566.

JURISDICTION AND VENUE

6. This action for patent infringement arises under the patent laws of the United States, Title 35 of the United States Code.

7. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

8. This Court has personal jurisdiction over defendant 10X because, *inter alia*, 10X is incorporated in Delaware, and committed, aided, abetted, induced, contributed to, and/or participated in the commission of tortious acts of patent infringement that have led to foreseeable harm and injury to Plaintiffs in Delaware, 10X has substantial contacts with the forum as a consequence of conducting business in Delaware.

9. Venue is proper in this District under 28 U.S.C. § 1400(b) because 10X is a Delaware corporation.

BACKGROUND

10. Cellular Research is a pioneering biotechnology research and development company founded in 2011 by innovators from Silicon Valley and Stanford University. Cellular Research's mission is to revolutionize life science research by enabling high resolution

investigation of single cells and limited biological samples. Cellular Research developed advanced tools for massively parallel single cell genetic analysis based on their proprietary Molecular Indexing™ technology to produce gene expression profiles from single cells. Its first two product lines Pixel™ and Precise™ delivered the power of Molecular Indexing™ to customers interested in high accuracy and precision for gene expression studies.

11. BD is a global medical technology company that is advancing the world of health by improving medical discovery, diagnostics and the delivery of care. BD leads in patient and healthcare worker safety and the technologies that enable medical research and clinical laboratories. The company provides innovative solutions, including products that help advance medical research and genomics, and enhance the diagnosis of infectious disease and cancer.

12. In 2015, BD acquired Cellular Research, which set the stage for the next generation of commercial tools in the field of single cell genomic analysis, widely acknowledged by leading academic and industry researchers as the next frontier of biological discovery and clinical advancement.

13. The BD Rhapsody™ Single Cell Analysis System leverages innovations from Cellular Research. The BD Rhapsody™ system enables digital quantitation of hundreds of expressed genes across tens of thousands of single cells, provides customized assays that are flexible enough to meet any experimental need, and comprises an efficient system that reduces experimentation time and sequencing costs.

14. BD's past and future success as a company rests on its ability to continuously bring new innovations to market, including innovations such as the BD Rhapsody™ system for genomic and gene expression analysis, and in protecting those innovations, including the inventions claimed in the Fodor and Fan patents.

15. The Asserted Patents relate to fundamental technologies for single molecule digital counting (Fodor patents) and single-cell multiplex analysis (Fan patents) platforms. The Asserted Patents contribute to BD's reputation as an industry leader in single molecule counting and single cell analysis technologies and help protect BD's significant investment to design and develop innovative solutions for its customers.

16. 10X has infringed and continues to infringe the Asserted Patents by making, using (including during research and development activities and product testing), offering for sale, selling and/or importing at least 10X's single cell solutions and workflows, or inducing or contributing to such acts.

17. 10X's infringement has been and continues to be willful. At least since about May 2017, 10X has had knowledge of the Asserted Patents, has recognized their value, and has also recognized that it needs a license to the Asserted Patents in order to make, use, sell, offer to sell and/or import at least its single cell solutions and workflows. 10X has not obtained such a license. Nevertheless, 10X has continued its infringement with knowledge of the Asserted Patents and recognition of its need for a license.

OVERVIEW OF 10X INFRINGING PRODUCTS

18. As examples, set forth below are preliminary exemplary descriptions detailing 10X's infringing products. These descriptions are not intended to limit Plaintiffs' right to amend, supplement or modify these descriptions or any other analysis, description, or claim chart or allege that other activities of 10X infringe the identified claims or any other claims of these patents or any other patents.

19. Defendant manufactures, uses, sells, offers for sale and/or imports instruments, kits, reagents, software, and parts and training kits combined into, *inter alia*, a "Single Cell Gene

Expression Solution" (hereinafter "Single Cell 3' Workflow") and a "Single Cell Immune Profiling Solution" (hereinafter "Single Cell 5' Workflow").

20. Defendant's Single Cell 3' Workflow and the Single Cell 5' Workflow are for profiling gene expression of single cells by assessing nucleic acid contents of cells and involve steps of labelling cellular nucleic acids with barcode nucleic acids, to thereby obtain information relating to mRNA expression profiles for individual genes in a cell.

SINGLE CELL 3' WORKFLOW ACCUSED PRODUCTS

21. Defendant's Single Cell 3' Workflow provides a "scalable solution for cell characterization and gene expression profiling of hundreds to millions of cells" that is used to perform "millions of parallel reactions to enable gene expression profiling at scale with single cell resolution."[1]

22. Defendant's Single Cell 3' Workflow is also known as "Single Cell Gene Expression," and "Chromium Single Cell 3'."

23. As shown in Defendant's own literature, Defendant itself markets, and sells various instruments, reagents, software, and parts and training kits as a single "solution" and describes that "solution" in a single "Product Sheet."

[1] https://www.10xgenomics.com/solutions/single-cell/

THE CHROMIUM SINGLE CELL GENE EXPRESSION SOLUTION

PRODUCTS	PRODUCT CODE
Chromium Single Cell 3' Library & Gel Bead Kit v2, 16 rxns	120237
Chromium Single Cell 3' Library & Gel Bead Kit v2, 4 rxns	120267
Chromium Single Cell A Chip Kit, 48 rxns	120236
Chromium Single Cell A Chip Kit, 16 rxns	1000009
Chromium i7 Multiplex Kit, 96 rxns	120262
Chromium Single Cell Controller & Accessory Kit, 12 Mo. Warranty	120263
Chromium Single Cell Controller & Accessory Kit, 24 Mo. Warranty	120212
Chromium Controller & Accessory Kit, 24 Mo. Warranty	120246
Chromium Controller & Accessory Kit, 12 Mo. Warranty	120223
Cell Ranger Analysis Pipelines go.10xgenomics.com/scRNA-3/cell-ranger	DOWNLOAD
Loupe Cell Browser go.10xgenomics.com/scRNA-3/loupe-cell	DOWNLOAD

24. On information and belief, reagents sold by Defendant for the Single Cell 3' Workflow include the "Chromium Single Cell 3' Library & Gel Bead Kit v2, 16 rxns" (Product ID 120237), the "Chromium Single Cell 3' Library & Gel Bead Kit v2, 4 rxns" (Product ID 120267), "Chromium Single Cell 3' Library Kit" (Product ID 120230), and the "Chromium Single Cell 3' Gel Bead Kit" (Product ID 120231).

25. On information and belief, the "Chromium Single Cell 3' Library & Gel Bead Kit v2, 16 rxns" (Product ID 120237) comprises the "Chromium Single Cell 3' Library Kit v2, 16

rxns" (Product ID 120234) and the "Chromium Single Cell 3' Gel Bead Kit v2, 16 rxns" (Product ID 120235).

26. On information and belief, the "Chromium Single Cell 3' Library Kit v2, 16 rxns" (Product ID 120234) comprises RT Reagent Mix (Product ID 220089), RT Enzyme Mix (Product ID 220079), Additive A (Product ID 220074), RT Primer (Product ID 310354), Buffer Sample Clean Up 1 (Product ID 220020), Amplification Master Mix (Product ID 220125), cDNA Primer Mix 1 (Product ID 220106), cDNA Additive 1 (Product ID 220067), Fragmentation Enzyme Blend (Product ID 220107), Fragmentation Buffer (Product ID 220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220110), Adaptor Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

27. On information and belief, the "Chromium Single Cell 3' Gel Bead Kit v2, 16 rxns" (Product ID 120235) comprises Single Cell 3' Gel Beads (Product ID 220104).

28. On information and belief, the "Chromium Single Cell 3' Library Kit" (Product ID 120230) comprises RT Reagent Mix (Product ID 220071), RT Enzyme Mix (Product ID 220070), RNase Inhibitor (Product ID 220065), Additive A (Product ID 220074), RT Primer (Product ID 310354), Buffer for Sample Clean Up (Product ID 220020), cDNA Primer Mix 1 (Product ID 220066), cDNA Additive 1 (Product ID 220067), Amplification Master Mix (Product ID 220073), End Repair and A-tailing Buffer (Product ID 220046), End Repair and A-tailing Enzyme (Product ID 220047), Ligation Buffer (Product ID 220048), DNA Ligase (Product ID 220049), R1 Adaptor Mix (Product ID 220064), and SI-PCR Primer (Product ID 220068), and Surrogate Fluid (Product ID 220021).

29. On information and belief, the "Chromium Single Cell 3' Gel Bead Kit" (Product ID 120231) comprises Single Cell 3' Gel Bead Strip (Product ID 220063).

30. On information and belief, the "Chromium Single Cell 3' Library & Gel Bead Kit v2, 4 rxns" (Product ID 120267) comprises the "Chromium™ Single Cell 3' Library Kit v2, 4 rxns" (Product ID 120264) and the "Chromium Single Cell 3' Gel Bead Kit v2, 4 rxns" (Product ID 120265).

31. On information and belief, the "Chromium™ Single Cell 3' Library Kit v2, 4 rxns" (Product ID 120264) comprises RT Reagent Mix (Product ID 220089), RT Enzyme Mix (Product ID 220127), Additive A (Product ID 220074), RT Primer (Product ID 310354), Buffer Sample Clean Up 1 (Product ID 220020), Amplification Master Mix 1 (Product ID 220129), cDNA Primer Mix 1 (Product ID 220106), cDNA Additive 1 (Product ID 220067), Fragmentation Enzyme Blend (Product ID 220130), Fragmentation Buffer (Product ID 220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220131), Adaptor Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

32. On information and belief, the "Chromium Single Cell 3' Gel Bead Kit v2, 4 rxns" (Product ID 120265) comprises Single Cell 3' Gel Beads (Product ID 220104).

33. On information and belief, additional reagents sold by Defendant for the Single Cell 3' Workflow include, the "Chromium Single Cell A Chip Kit, 48 rxns" (Product ID 120236), the "Chromium Single Cell A Chip Kit, 16 rxns" (Product ID 1000009), the "Chromium Multiplex Kit, 96 rxns" (Product ID 120262), the "Chromium Single Cell 3' Chip Kit" (Product ID 120232).

34. On information and belief, the "Chromium Single Cell A Chip Kit, 48 rxns" (Product ID 120236) comprises Single Cell A Chip (Product ID 230027), Gaskets (Product ID 370017), Partitioning Oil (Product ID 220088), and Recovery Agent (Product ID 220016).

35. On information and belief, the "Chromium Single Cell A Chip Kit, 16 rxns" (Product ID 1000009) comprises Single Cell A Chip (Product ID 2000019), Gaskets (Product ID 3000072), Partitioning Oil (Product ID 220088), and Recovery Agent (Product ID 220016).

36. On information and belief, the "Chromium Multiplex Kit, 96 rxns" (Product ID 120262) comprises the Chromium™ i7 Sample Index Plate (Product ID 220103).

37. On information and belief, the "Chromium Single Cell 3' Chip Kit" (Product ID 120232) comprises Single Cell 3' Chips (Product ID 230008), Gaskets (Product ID 370017), Partitioning Oil (Product ID 220017), and Recovery Agent (Product ID 220016).

38. On information and belief, parts and training kits sold by Defendant for the Single Cell 3' Workflow include the "Chromium Training Chip Kit" (Product ID 120244), and the "Chromium Training Reagents and Gel Bead Kit" (Product ID 120238).

39. On information and belief, instruments sold by Defendant for the Single Cell 3' Workflow include the "Chromium Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120223 or 120246) and the "Chromium Single Cell Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120263 or 120212).

40. On information and belief, the "Chromium Controller Accessory Kit" (Product ID 110204) comprises Power Cord (Product ID 34000X), 10x™ Vortex Adapter (Product ID 330002), 10x™ Chip Holder (Product ID 330019), 10x™ Vortex Clip (Product ID 230002), 10x™ Magnetic Separator (Product ID 230003), and Chromium Test Chip V1 (Product ID 230024).

41. The term "**Single Cell 3' Workflow Accused Products**" is used hereinafter to refer to the foregoing instruments, reagents, software, and parts and training kits sold or provided by Defendant for the Single Cell 3' Workflow.

SINGLE CELL 5' WORKFLOW ACCUSED PRODUCTS

42. On information and belief, Defendant's Single Cell 5' Workflow provides an "approach to simultaneously examine the cellular context of the adaptive immune response and the immune repertoires of hundreds to millions of T and B cells on a cell-by-cell basis" that is used to "identify cell-type-specific immune repertoires on a cell-by-cell basis."[2]

43. On information and belief, Defendant's Single Cell 5' Workflow is also known as "Single Cell Immune Profiling," and "Chromium Single Cell V(D)J."

44. As shown in Defendant's own literature, Defendant itself markets, and sells various instruments, reagents, software, and parts and training kits as a single "solution" and describes that "solution" in a single "Product Sheet."

[2] https://www.10xgenomics.com/solutions/vdj/

THE CHROMIUM SINGLE CELL IMMUNE PROFILING SOLUTION

Gene Expression & Immune Repertoire Profiling

REAGENT KITS	PRODUCT CODE
Chromium Single Cell 5' Library & Gel Bead Kit, 16 rxns	1000006
Chromium Single Cell 5' Library & Gel Bead Kit, 4 rxns	1000014
Chromium Single Cell A Chip Kit, 48 rxns	120236
Chromium Single Cell A Chip Kit, 16 rxns	1000009
Chromium i7 Multiplex Kit, 96 rxns	120262
Chromium Single Cell 5' Library Construction Kit, 16 rxns*	1000020
Target Enrichment Kits	*See Enrichment Kits*

* Library & Gel Bead Kit contains reagents to generate one library type (Gene Expression, TCR or Ig) from one Gel Bead reaction. Each additional library type from the same Gel Bead reaction requires additional reactions from the 5' Library Construction Kit

Target Enrichment Kits

SPECIES & TARGET	ENRICHMENT KITS	PRODUCT CODE
Human T cells	Chromium Single Cell V(D)J Enrichment Kit, Human T Cell, 96 rxns	1000005
Human B Cells	Chromium Single Cell V(D)J Enrichment Kit, Human B Cell, 96 rxns	1000016
Mouse T Cells	Chromium Single Cell V(D)J Enrichment Kit, Mouse T Cell, 96 rxns	1000071
Mouse B Cells	Chromium Single Cell V(D)J Enrichment Kit, Mouse B Cell, 96 rxns	1000072

Immune Repertoire Profiling

REAGENT KITS	PRODUCT CODE
Chromium Single Cell 5' Library & Gel Bead Kit, 16 rxns	1000006
Chromium Single Cell 5' Library & Gel Bead Kit, 4 rxns	1000014
Chromium Single Cell A Chip Kit, 48 rxns	120236
Chromium Single Cell A Chip Kit, 16 rxns	1000009
Chromium i7 Multiplex Kit, 96 rxns	120262
Target Enrichment Kits	*See Enrichment Kits*

CONTROLLERS & SOFTWARE	PRODUCT CODE
Chromium Single Cell Controller & Accessory Kit, 12 Mo. Warranty	120263
Chromium Single Cell Controller & Accessory Kit, 24 Mo. Warranty	120212
Chromium Controller & Accessory Kit, 24 Mo. Warranty	120246
Chromium Controller & Accessory Kit, 12 Mo. Warranty	120223
Cell Ranger Analysis Pipelines go.10xgenomics.com/vdj/cell-ranger	DOWNLOAD
Loupe V(D)J Browser go.10xgenomics.com/vdj/loupe-vdj	DOWNLOAD
Loupe Cell Browser go.10xgenomics.com/vdj/loupe-cell	DOWNLOAD

PRODUCTS	PRODUCT CODE
Chromium Single Cell 5' Library Construction Kit, 16 rxns	1000020
Chromium Single Cell 5' Library & Gel Bead Kit, 16 rxns	1000006
Chromium Single Cell 5' Library & Gel Bead Kit, 4 rxns	1000014
Chromium Single Cell V(D)J Enrichment Kit, Human T Cell, 96 rxns	1000005
Chromium Single Cell V(D)J Enrichment Kit, Human B Cell, 96 rxns	1000016
Chromium Single Cell V(D)J Enrichment Kit, Mouse T Cell, 96 rxns	1000071
Chromium Single Cell V(D)J Enrichment Kit, Mouse B Cell, 96 rxns	1000072
Chromium i7 Multiplex Kit, 96 rxns	120262
Chromium i7 Multiplex Kit N, Set A, 96 rxns	1000084
Chromium Single Cell A Chip Kit, 16 rxns	1000009
Chromium Single Cell A Chip Kit, 48 rxns	120236
Chromium Single Cell 5' Feature Barcode Library Kit, 16 rxns	1000080
Chromium Single Cell Controller & Accessory Kit, 12 Mo. Warranty	120263
Chromium Single Cell Controller & Accessory Kit, 24 Mo. Warranty	120212
Chromium Controller & Accessory Kit, 12 Mo. Warranty	120223
Chromium Controller & Accessory Kit, 24 Mo. Warranty	120246
Cell Ranger	go.10xgenomics.com/vdj/cell-ranger
Loupe Cell Browser	go.10xgenomics.com/vdj/loupe-cell
Loupe V(D)J Browser	go.10xgenomics.com/vdj/loupe-vdj
Compatible Partner Product: Biolegend TotalSeq™-C	go.10xgenomics.com/totalseq-C
Compatible Partner Product: Immudex dCODE™ Dextramers®	go.10xgenomics.com/dCODE-Dextramers

45. On information and belief, reagents sold by Defendant for the Single Cell 5' Workflow include the "Chromium Single Cell 5' Library & Gel Bead Kit, 16 rxns" (Product ID 1000006), the "Chromium Single Cell 5' Library & Gel Bead Kit, 4 rxns" (Product ID 1000014).

46. On information and belief, the "Chromium Single Cell 5' Library & Gel Bead Kit, 16 rxns" (Product ID 1000006) comprises the "Chromium™ Single Cell 5' Library Kit, 16 rxns" (Product ID 1000002) and the "Chromium™ Single Cell 5' Gel Bead Kit, 16 rxns" (Product ID 1000003).

47. On information and belief, the "Chromium™ Single Cell 5' Library Kit, 16 rxns" (Product ID 1000002) comprises RT Reagent Mix 1 (Product ID 220089), RT Enzyme Mix B (Product ID 2000010), Additive A (Product ID 220074), Poly-dT RT Primer (Product ID 2000007), Buffer Sample Clean Up 1 (Product ID 220020), Amplification Master Mix (Product ID 220125), cDNA Primer Mix (Product ID 220106), cDNA Additive (Product ID 220067) , Fragmentation Enzyme Blend (Product ID 220107), Fragmentation Buffer (Product ID 220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220110), Adaptor Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

48. On information and belief, the "Chromium™ Single Cell 5' Gel Bead Kit, 16 rxns" (Product ID 1000003) comprises Single Cell 5' Gel Beads (Product ID 220112).

49. On information and belief, the "Chromium Single Cell 5' Library & Gel Bead Kit, 4 rxns" (Product ID 1000014) comprises the Chromium™ Single Cell 5' Library Kit, 4 rxns (Product ID 1000001) and the Chromium™ Single Cell 5' Gel Bead Kit, 4 rxns (Product ID 1000010).

50. On information and belief, the "Chromium™ Single Cell 5' Library Kit, 4 rxns" (Product ID 1000001) comprises RT Reagent Mix 1 (Product ID 220089), RT Enzyme Mix B (Product ID 2000021), Additive A (Product ID 220074), Poly-dT RT Primer (Product ID 2000007), Buffer Sample Clean Up 1 (Product ID 220020), Amplification Master Mix (Product ID 220125), cDNA Primer Mix (Product ID 220106), cDNA Additive (Product ID 220067) , Fragmentation Enzyme Blend (Product ID 220130), Fragmentation Buffer (Product ID 220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220131), Adaptor Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

51. On information and belief, the "Chromium™ Single Cell 5' Gel Bead Kit, 4 rxns" (Product ID 1000010) comprises Single Cell 5' Gel Beads (Product ID 220112).

52. On information and belief, additional reagents sold by Defendant for the Single Cell 5' Workflow include, the "Chromium Single Cell 3'/5' Library Construction Kit, 16 rxns" (Product ID 1000020), the "Chromium Single Cell V(D)J Enrichment Kit, Human T Cell, 96 rxns" (Product ID 1000005), the "Chromium Single Cell V(D)J Enrichment Kit, Human B Cell, 96 rxns" (Product ID 1000016), the "Chromium Single Cell A Chip Kit, 48 rxns" (Product ID 120236), the "Chromium Single Cell A Chip Kit, 16 rxns" (Product ID 1000009), the "Chromium Multiplex Kit, 96 rxns" (Product ID 120262), the "Chromium i7 Multiplex Kit N, Set A, 96 rxns" (Product ID 1000084), the "Chromium Single Cell V(D)J Enrichment Kit, Mouse B Cell, 96 rxns" (Product ID 1000072), the "Chromium Single Cell V(D)J Enrichment Kit, Mouse T Cell, 96 rxns" (Product ID 1000071).

53. On information and belief, the "Chromium Single Cell 3'/5' Library Construction Kit, 16 rxns" (Product ID 1000020) comprises "cDNA Additive" (Product ID 220067), Fragmentation Enzyme Blend (Product ID 220107), "Fragmentation Buffer (Product ID

220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220110), Amplification Master Mix (Product ID 220125), Adapter Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

54. On information and belief, the "Chromium Single Cell V(D)J Enrichment Kit, Human T Cell, 96 rxns" (Product ID 1000005) comprises cDNA Additive (Product ID 220067), Fragmentation Enzyme Blend (Product ID 220107), Fragmentation Buffer (Product ID 220108), Ligation Buffer (Product ID 220109), DNA Ligase (Product ID 220110), Amplification Master Mix (Product ID 220125), Adapter Mix (Product ID 220026), and SI-PCR Primer (Product ID 220111).

55. On information and belief, the "Chromium Single Cell V(D)J Enrichment Kit, Human B Cell, 96 rxns" (Product ID 1000016) comprises "Human B Cell Mix 1" (Product ID 2000035), and "Human B Cell Mix 2" (Product ID 2000036).

56. On information and belief, the "Chromium Single Cell A Chip Kit, 48 rxns" (Product ID 120236) comprises Single Cell A Chip (Product ID 230027), Gaskets (Product ID 370017), Partitioning Oil (Product ID 220088), and Recovery Agent (Product ID 220016).

57. On information and belief, the "Chromium Single Cell A Chip Kit, 16 rxns" (Product ID 1000009) comprises Single Cell A Chip (Product ID 2000019), Gaskets (Product ID 3000072), Partitioning Oil (Product ID 220088), and Recovery Agent (Product ID 220016).

58. On information and belief, the "Chromium Multiplex Kit, 96 rxns" (Product ID 120262) comprises the Chromium™ i7 Sample Index Plate (Product ID 220103).

59. On information and belief, the "Chromium Single Cell V(D)J Enrichment Kit, Mouse B Cell, 96 rxns" (Product ID 1000072) comprises "Mouse B Cell Mix 1" (Product ID 2000080), and "Mouse B Cell Mix 2" (Product ID 2000081).

60. On information and belief, the "Chromium Single Cell V(D)J Enrichment Kit, Mouse T Cell, 96 rxns" (Product ID 1000071) comprises "Mouse T Cell Mix 1" (Product ID 2000075), and "Mouse T Cell Mix 2" (Product ID 2000079).

61. On information and belief, parts and training kits sold by Defendant for the Single Cell 5' Workflow include the "Chromium Training Chip Kit" (Product ID 120244), and the Chromium Training Reagents and Gel Bead Kit" (Product ID 120238).

62. On information and belief, instruments sold by Defendant for the Single Cell 5' Workflow include the "Chromium Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120223 or 120246) and the "Chromium Single Cell Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120263 or 120212).

63. On information and belief, the "Chromium Controller Accessory Kit" (Product ID 110204) comprises Power Cord (Product ID 34000X), 10x™ Vortex Adapter (Product ID 330002), 10x™ Chip Holder (Product ID 330019), 10x™ Vortex Clip (Product ID 230002), 10x™ Magnetic Separator (Product ID 230003), and Chromium Test Chip V1 (Product ID 230024).

64. On information and belief, Defendant also make available software for use in connection with the Single Cell 3' Workflow and Single Cell 5' Workflow including "Cell Ranger," "Loupe Cell Browser," and "Loupe V(D)J Browser."

65. The term "**Single Cell 5' Workflow Accused Products**" is used hereinafter to refer to the foregoing instruments, reagents, software, and parts and training kits sold or provided by Defendant for the Single Cell 5' Workflow.

66. The term "Representative Accused Products" or "Accused Products" is used herein to refer to "Single Cell 3' Workflow Accused Products" and "Single Cell 5' Workflow

Accused Products." 10X has infringed and continues to infringe directly and/or indirectly, literally or under the doctrine of equivalents, the Asserted Patents by making, using (including during research and development activities and product testing), offering for sale, selling and/or importing at least the Accused Products, or inducing or contributing to such acts.

ADDITIONAL ACCUSED SINGLE CELL WORKFLOW PRODUCTS

67. Defendant also manufactures, uses, sells, offers for sale and/or imports instruments, kits, reagents, software and parts and training kits combined into, *inter alia*, a "Chromium Single Cell ATAC Solution" (hereinafter "Single Cell ATAC Workflow") and "Chromium Single Cell CNV Solution" (hereinafter "Single Cell CNV Workflow"), and "Chromium Single Cell Gene Expression Solution v3" (hereinafter "Single Cell 3' Workflow v3").

68. With respect to Defendant's Single Cell ATAC Workflow, Defendant itself markets, and sells various instruments, reagents, software, and parts and training kits as a single "solution" and describes that "solution" in a single "Product Sheet."[3]

[3] PS028_SingleCell_ATAC

PRODUCTS	PRODUCT CODE
Chromium Single Cell ATAC Library & Gel Bead Kit, 16 rxns	1000110
Chromium Single Cell ATAC Library & Gel Bead Kit, 4 rxns	1000111
Chromium Single Cell ATAC Chip E Kit, 48 rxn	1000082
Chromium Single Cell ATAC Chip E Kit, 16 rxn	1000086
Chromium i7 Multiplex Kit N, Set A, 96 rxn	1000084
Chromium Single Cell Controller & Accessory Kit, 12 Mo. Warranty	120263
Chromium Single Cell Controller & Accessory Kit, 24 Mo. Warranty	120212
Chromium Controller & Accessory Kit, 24 Mo. Warranty	120246
Chromium Controller & Accessory Kit, 12 Mo. Warranty	120223
Cell Ranger ATAC Pipeline go.10xgenomics.com/scATAC/cell-ranger-ATAC	DOWNLOAD
Loupe Cell Browser go.10xgenomics.com/scATAC/loupe-cell	DOWNLOAD

69. On information and belief, reagents sold by Defendant for the Single Cell ATAC Workflow include the "Chromium Single Cell ATAC Library & Gel Bead Kit, 16 rxns" (Product ID 1000110), and the "Chromium Single Cell ATAC Library & Gel Bead Kit, 4 rxns" (Product ID 1000111).

70. On information and belief, additional reagents sold by Defendant for the Single Cell ATAC Workflow include, the "Chromium Single Cell ATAC Chip E Kit, 48 rxn" (Product ID 1000082), the "Chromium Single Cell ATAC Chip E Kit, 16 rxn" (Product ID 1000086), the "Chromium i7 Multiplex Kit N, Set A, 96 rxn" (Product ID 1000084).

71. On information and belief, instruments sold by Defendant for the Single Cell ATAC Workflow include the "Chromium Controller & Accessory Kit" with 12 or 24 month

warranty (Product ID 120223 or 120246) and the "Chromium Single Cell Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120263 or 120212).

72. On information and belief, the "Chromium Controller Accessory Kit" (Product ID 110204) comprises Power Cord (Product ID 34000X), 10x™ Vortex Adapter (Product ID 330002), 10x™ Chip Holder (Product ID 330019), 10x™ Vortex Clip (Product ID 230002), 10x™ Magnetic Separator (Product ID 230003), and Chromium Test Chip V1 (Product ID 230024).

73. With respect to Defendant's Single Cell CNV Workflow, Defendant itself markets, and sells various instruments, reagents, software, and parts and training kits as a single "solution" and describes that "solution" in a single "Product Sheet."[4]

[4] PS023_SingleCellCNV_ProductSheet

The Chromium Single Cell CNV Solution

PRODUCTS	PRODUCT CODE
Chromium Single Cell DNA Cell Bead Kit, 16 rxns	1000056
Chromium Single Cell DNA Library & Gel Bead Kit, 16 rxns	1000040
Chromium Chip C Single Cell DNA Kit, 48 rxns	1000022
Chromium Chip D Single Cell DNA Kit, 48 rxns	1000042
Chromium i7 Multiplex Kit, 96 rxns	120262
Flowmi Filters, 50 rxns	1000055
10x Chromium Chip D Holder	1000053
10x Magnetic Separator A	1000054
Chromium Single Cell Controller & Accessory Kit, 12 Mo. Warranty	120263
Chromium Single Cell Controller & Accessory Kit, 24 Mo. Warranty	120212
Chromium Controller & Accessory Kit, 24 Mo. Warranty	120246
Chromium Controller & Accessory Kit, 12 Mo. Warranty	120223
Cell Ranger DNA Analysis Pipelines	DOWNLOAD
Loupe scDNA Browser	DOWNLOAD

74. On information and belief, reagents sold by Defendant for the Single Cell CNV Workflow include the "Chromium Single Cell DNA Cell Bead Kit, 16rxn" (Product ID 1000056), and the "Chromium Single Cell DNA Library and Gel Bead Kit, 16 rxn" (Product ID 1000040).

75. On information and belief, additional reagents sold by Defendant for the Single Cell CNV Workflow include, the "Chromium Chip C Single Cell DNA Kit, 48rxn" (Product ID 1000022), the "Chromium Chip D Single Cell DNA Kit, 48rxn" (Product ID 1000042), the

"Chromium i7 Multiplex Kit, 96 rxns" (Product ID 120262), the "Flowmi Filter, 50 rxns" (Product ID 1000055), the "10x Chromium Chip D Holder" (Product ID 1000053), and the "10x Magnetic Separator A" (Product ID 1000054)

76. On information and belief, instruments sold by Defendant for the Single Cell CNV Workflow include the "Chromium Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120223 or 120246) and the "Chromium Single Cell Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120263 or 120212).

77. On information and belief, the "Chromium Controller Accessory Kit" (Product ID 110204) comprises Power Cord (Product ID 34000X), 10x™ Vortex Adapter (Product ID 330002), 10x™ Chip Holder (Product ID 330019), 10x™ Vortex Clip (Product ID 230002), 10x™ Magnetic Separator (Product ID 230003), and Chromium Test Chip V1 (Product ID 230024).

78. With respect to Defendant's Single Cell 3' Workflow v3, Defendant itself markets, and sells various instruments, reagents, software, and parts and training kits as a single "solution."[5]

[5] https://www.10xgenomics.com/product-list/#single-cell

Chromium Single Cell Gene Expression Solution

To view a list of products by application type, first select your desired version of the Single Cell Gene Expression Solution. If you would like to combine this solution with Feature Barcoding technology, select Feature Barcode type(s).

Gene Expression Version

- (●) Gene Expression v3
- ( ) Gene Expression v2

Feature Barcode Selection

- [ ] None
- [ ] Cell Surface Protein
- [ ] CRISPR Screening
- [ ] Other

Reagents & Consumables	Reactions	Product Code
Chromium Chip B Single Cell Kit	48 rxns	1000073
Chromium Chip B Single Cell Kit	16 rxns	1000074
Chromium i7 Multiplex Kit	96 rxns	120262
Chromium Single Cell 3′ Feature Barcode Library Kit	16 rxns	1000079
Chromium Single Cell 3′ Library & Gel Bead Kit v3	4 rxns	1000092
Chromium Single Cell 3′ Library & Gel Bead Kit v3	16 rxns	1000075

Compatible Partner Products		
Biolegend TotalSeq™- B		Learn More

Instruments	Warranty	Product Code
Chromium Controller & Accessory Kit	12 months	120223
Chromium Controller & Accessory Kit	24 months	120246
Chromium Single Cell Controller & Accessory Kit	12 months	120263
Chromium Single Cell Controller & Accessory Kit	24 months	120212

Analysis Software	
Cell Ranger Analysis Pipelines	Download
Loupe Cell Browser	Download

Documentation	
Demonstrated Protocol – Antibody Staining of Cells	Coming soon
User Guide for Gene Expression & CRISPR Screening	Coming soon
User Guide for Gene Expression v3	Coming soon

79. On information and belief, reagents sold by Defendant for the Single Cell 3' Workflow v3 include the "Chromium Single Cell 3′ Feature Barcode Library Kit 16 rxns"

(Product ID 10000401000079), the "Chromium Single Cell 3′ Library & Gel Bead Kit v34 rxns" (Product ID 10000401000092), and the "Chromium Single Cell 3′ Library & Gel Bead Kit v316 rxns" (Product ID 10000401000075).

80. On information and belief, additional reagents sold by Defendant for the Single Cell 3' Workflow v3 include, the "Chromium Chip B Single Cell Kit 48 rxns" (Product ID 1000073), the "Chromium Chip B Single Cell Kit 16 rxns" (Product ID 1000074), and the "Chromium i7 Multiplex Kit 96 rxns" (Product ID 120262).

81. On information and belief, instruments sold by Defendant for the Single Cell 3' Workflow v3 include the "Chromium Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120223 or 120246) and the "Chromium Single Cell Controller & Accessory Kit" with 12 or 24 month warranty (Product ID 120263 or 120212).

82. On information and belief, the "Chromium Controller Accessory Kit" (Product ID 110204) comprises Power Cord (Product ID 34000X), 10x™ Vortex Adapter (Product ID 330002), 10x™ Chip Holder (Product ID 330019), 10x™ Vortex Clip (Product ID 230002), 10x™ Magnetic Separator (Product ID 230003), and Chromium Test Chip V1 (Product ID 230024).

83. On information and belief, the Single Cell ATAC Workflow, the Single Cell CNV Workflow, and the Single Cell 3' Workflow v3 operate in substantially and materially the same way as the Accused Products.

84. 10X has infringed and continues to infringe directly and/or indirectly, literally or under the doctrine of equivalents, the Asserted Patents by making, using (including during research and development activities and product testing), offering for sale, selling and/or

importing at least the Single Cell ATAC Workflow, the Single Cell CNV Workflow, and the Single Cell 3' Workflow v3, or inducing or contributing to such acts.

COUNT 1
(INFRINGEMENT OF THE '358 PATENT)

85. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

86. U.S. Patent No. 8,835,358 (the "'358 patent"), entitled "Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels," was duly and legally issued on September 16, 2014 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the '358 patent is attached as **Exhibit 1**.

87. The invention of the '358 patent is directed in general to methods for attaching nucleic acid label tags to nucleic acid molecules in a sample, amplifying, and detecting at least a portion of the nucleic acid molecules and attached nucleic acid label tag. In certain aspects of the invention, the attaching can comprise reverse transcription.

88. Claim 6 of the '358 patent, reproduced below, is representative:

6. A method comprising:

(a) combining a mixture comprising at least two distinct target nucleic acid molecules with a pool of nucleic acid label-tags, wherein the pool of nucleic acid label-tags comprises a plurality of nucleic acid label-tags with different sequences;

(b) attaching at least two nucleic acid label-tags from the pool of nucleic acid label-tags to the at least two distinct target nucleic acid molecules to obtain at least two label-tag-target nucleic acid molecules, wherein the distinct target nucleic acid molecules have different sequences from one another;

(c) amplifying at least a portion of the label-tag-target nucleic acid molecules, wherein an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule; and

(d) detecting an amplified product of step (c).

89. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ' 358 patent, including at least claim 6 of the '358 patent, directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

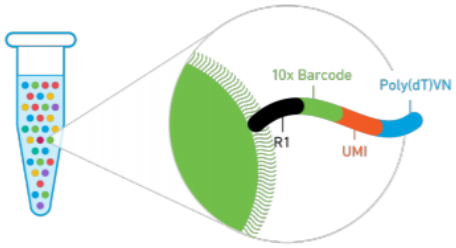
90. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 6 of the '358 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD's ability to demonstrate Defendant's direct, indirect, literal, or equivalent infringement of additional '358 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

91. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, "combining a mixture comprising at least two distinct target nucleic acid molecules with a pool of nucleic acid label-tags" as recited in step (a) of claim 6 of the '358 patent occurs because "[t]he 10x™ GemCode™ Technology… partition[s] thousands of cells into nanoliter-scale Gel

Bead-In-EMulsions (GEMs),"[6] and "[o]nce partitioned, the Gel Bead dissolves and its oligo primers are released into the aqueous environment of the GEM."[7] The "combining" recited in step (a) of claim 6 of the '358 patent occurs when "the cell captured in the GEM is […] lysed" (thereby releasing the "at least two distinct target nucleic acid molecules" in the cell) and "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction"[8] which is "a mixture comprising at least two distinct target nucleic acid molecules with a pool of nucleic acid label-tags."

92. The oligos of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown below[9]:

Each Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1):



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

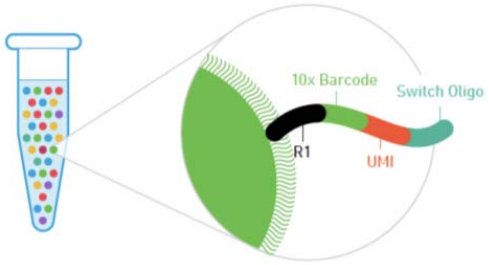
Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.

[6] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[7] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[8] *Id.*

[9] *Id.*



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

93. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products "wherein the pool of nucleic acid label-tags comprises a plurality of nucleic acid label-tags with different sequences" as recited in step (a) of claim 6 exists because each of the GEMs "contain millions of oligo primers that comprise different Unique Molecular Identifiers"[10] that make up "a pool of ~ 750000 barcodes to separately index each cell's transcriptome."[11]

94. In the **Single Cell 3' Workflow** Accused Products, the "attaching at least two nucleic acid label-tags from the pool of nucleic acid label-tags to the at least two distinct target nucleic acid molecules to obtain at least two label-tag-target nucleic acid molecules, wherein the distinct target nucleic acid molecules have different sequences from one another" recited in step (b) of the '358 patent occurs when "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts" and a "reverse transcription reaction is primed by the barcoded Gel Bead oligo and the reverse transcriptase incorporates the template switch oligo via a template switching reaction at the 5' end of the transcript."[12] As illustrated below[13], this reverse

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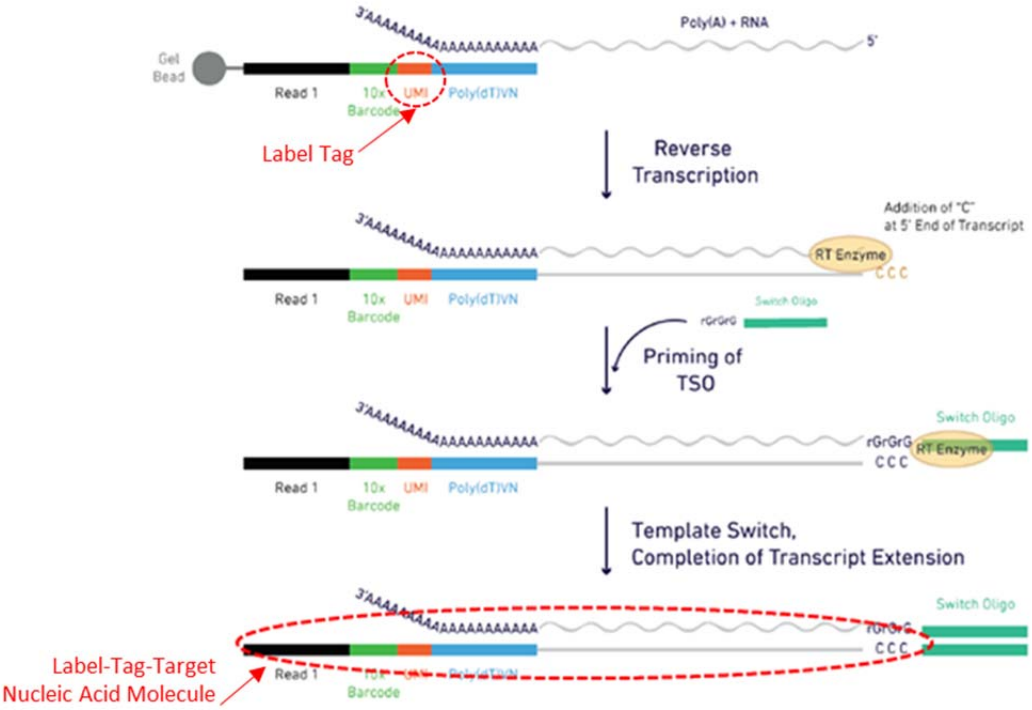
10 *Id.*

11 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf; "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

12 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

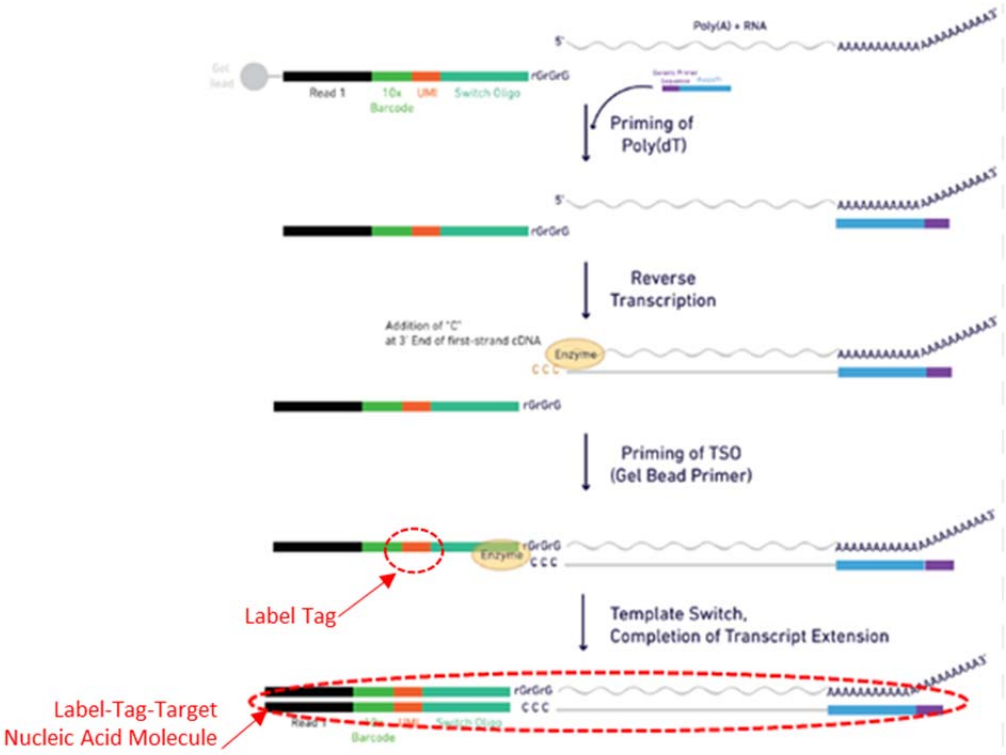
transcription reaction is primed by a poly(dT) sequence on the oligo, thus yielding "at least two label-tag-target nucleic acid molecules, wherein the distinct target nucleic acid molecules have different sequences from one another."



95. In the **Single Cell 5' Workflow** Accused Products, the "attaching at least two nucleic acid label-tags from the pool of nucleic acid label-tags to the at least two distinct target nucleic acid molecules to obtain at least two label-tag-target nucleic acid molecules, wherein the distinct target nucleic acid molecules have different sequences from one another" recited in step (b) of the '358 patent occurs when "[t]he contents of the GEM (oligos, lysed cell components and Master Mix that contains the Poly-dT RT primer) are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from the poly-adenylated mRNA" and "[t]he reverse transcriptase incorporates the Gel Bead oligo via a template switching reaction at

[13] *Id.* at Figure 3 (cropped, markings added)

the 5' end of the transcript."[14] Here, as shown below,[15] the reverse transcription product comprises a polyC tail which is hybridized to the barcoded Gel Bead oligo to thereby result in attachment to "distinct target nucleic acid molecules have different sequences from one another."



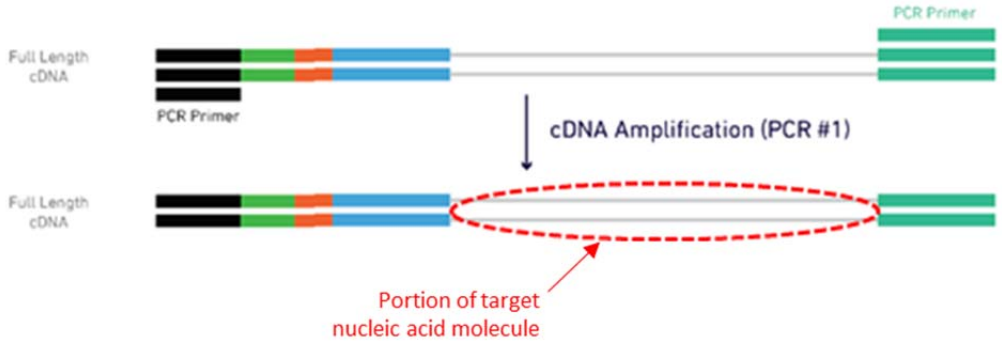
96. In the **Single Cell 3' Workflow** Accused Products, the "amplifying at least a portion of the label-tag-target nucleic acid molecules wherein an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule" as recited in step (c) of claim 6 of the '358 patent occurs because "[t]he GEMs are then 'broken', pooling single-stranded, barcoded cDNA molecules from every cell" and "[a] bulk PCR-amplification and Enzymatic Fragmentation" follows.[16] As illustrated below[17], this

[14] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

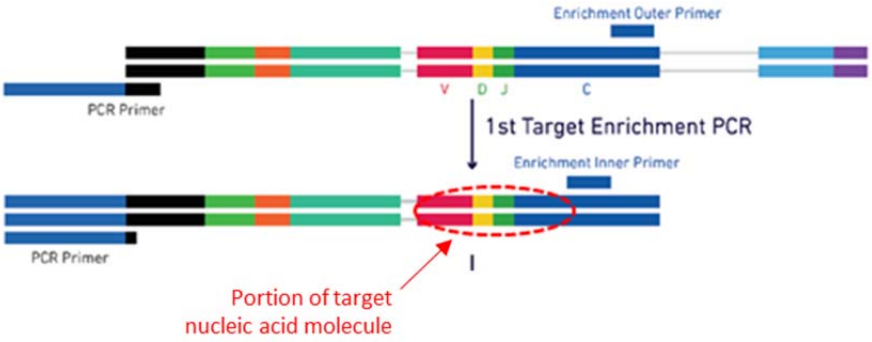
[15] *Id.* at Figure 3 (cropped, markings added)

[16] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

amplification step results in products wherein "an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule."



97. In the **Single Cell 5' Workflow** Accused Products, the "amplifying at least a portion of the label-tag-target nucleic acid molecules wherein an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule" as recited in step (c) of claim 6 of the '358 patent occurs because "[t]he Single Cell V(D)J Solution offers the option to generate" by PCR amplification, "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[18] As illustrated below[19], the Direct Target Enrichment option results in products wherein "an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule."



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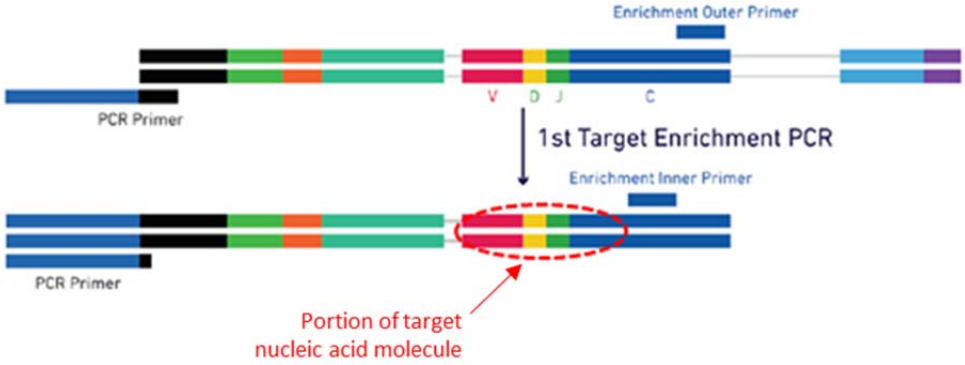
[17] *Id.* at Figure 3 (cropped, markings added)

[18] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[19] *Id.* at Figure 3 (cropped, markings added)

98. As illustrated below[20], the cDNA Amplification followed by Target Enrichment option in the **Single Cell 5' Workflow** Accused Products also results in products wherein "an amplified portion of the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule."



99. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, the "detecting an amplified product of step (c)" as recited in step (d) occurs because "[t]he Single Cell 3' Protocol produces Illumina-ready sequencing libraries" [21] and "[t]he Single Cell V(D)J Solutions produce V(D)J enriched and 5' gene expression Illumina-ready sequencing libraries."[22] Once these libraries are "generated and sequenced," "the 10x Barcodes are used to associate individual reads back to the individual partitions."[23]

100. 10X has also induced and currently induces infringement of at least claim 6 of the '358 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along

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[20] *Id.* at Figure 4 (cropped, markings added)

[21] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

[22] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[23] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 6 of the '358 patent.[24] 10X has known of the '358 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '358 patent.

101. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 6 of the '358 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 6 of the '358 patent.[25] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according to at least claim 6 of the '358 patent, and especially made and adapted for use in a manner that infringes at least claim 6 of the '358 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 6 of the '358 patent. 10X has knowledge of the '358 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '358 patent.

102. Defendant's infringement has been willful and deliberate because Defendant has known of the '358 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '358 patent.

103. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive

[24] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[25] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages, injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 2
(INFRINGEMENT OF THE '857 PATENT)

104. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

105. U.S. Patent No. 9,315,857 (the "'857 patent"), entitled "Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels," was duly and legally issued on April 19, 2016 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the '857 patent is attached as **Exhibit 2**.

106. The invention of the '857 patent is directed in general to methods for determining the number of copies of a nucleic acid target by attaching a plurality of diverse label-tags to a nucleic acid target from a sample, amplifying the plurality of labeled-targets, and detecting the plurality of amplified labeled-targets.

107. Claim 1 of the '857 patent, reproduced below, is representative:

1. A method comprising:

a) attaching a plurality of diverse label-tags to a nucleic acid target from a sample that contains multiple copies of the nucleic acid target, thereby producing a plurality of labeled targets, wherein:

i) a label-tag of the plurality of diverse label-tags comprises nucleotides selected from purine bases, pyrimidine bases, natural nucleotide bases, chemically modified nucleotide bases, biochemically modified nucleotide bases, non-natural nucleotide bases; and

ii) a labeled target of the plurality of labeled targets comprises a distinct label-tag and at least a portion of a nucleic acid target, or its complementary sequence;

b) amplifying the plurality of labeled-targets to produce a plurality of amplified labeled-targets, wherein an amplified labeled-target of the plurality of amplified labeled-targets comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag; and

c) detecting the plurality of amplified labeled-targets by sequencing at least a portion of the target and the label-tag; and

d) determining the number of copies of the nucleic acid target, as indicated by the number of different label-tags that are associated with the nucleic acid target.

108. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’857 patent, including at least claim 1 of the ’857 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

109. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ’857 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate

Defendant's direct, indirect, literal, or equivalent infringement of additional '857 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

110. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, the "attaching a plurality of diverse label-tags to a nucleic acid target from a sample that contains multiple copies of the nucleic acid target" as recited in step (a) of claim 1 occurs because the label tags employed in the attaching step are from GEMs that "contain millions of oligo primers" [26] that comprise different "Unique Molecular Identifiers" that make up "a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[27] and because "[t]he cell captured in the GEM is also lysed."[28] The poly A-tailed mRNA transcripts[29] of a cell are the "multiple copies of the nucleic acid target." The oligos of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown below[30]:

[26] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

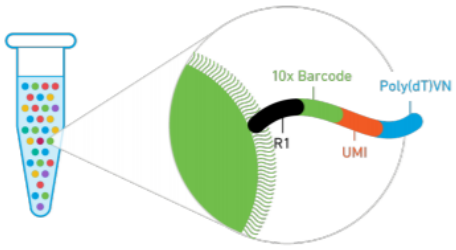
[27] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[28] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[29] *Id.*

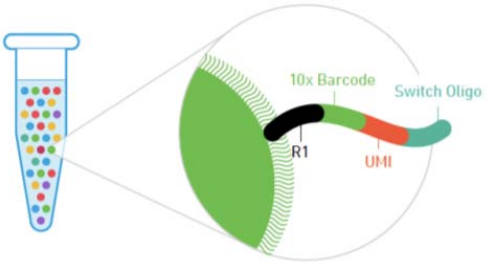
[30] *Id.*

Each Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1):



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



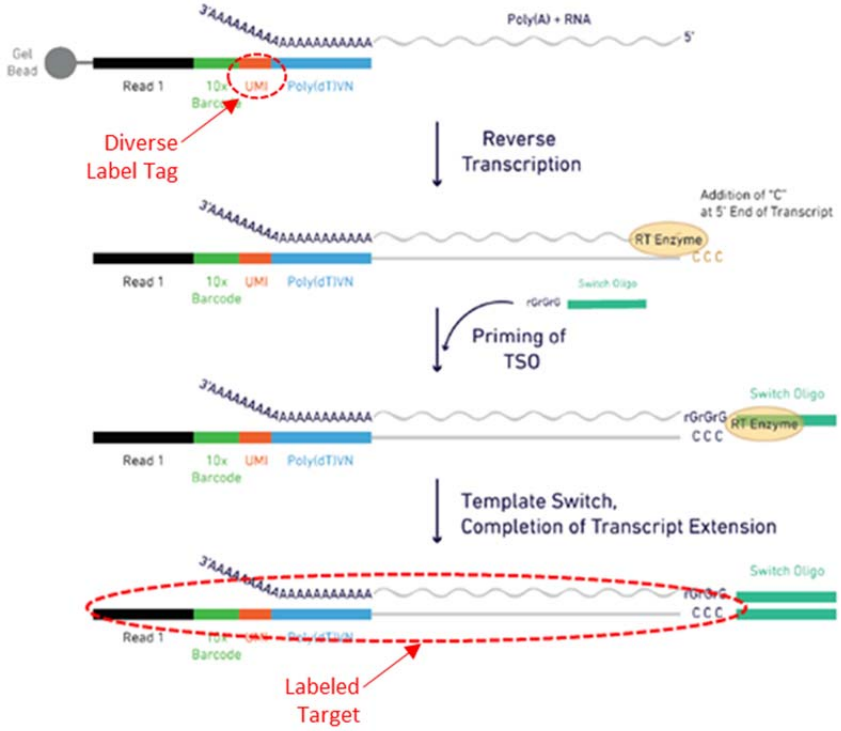
i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

111. In the **Single Cell 3' Workflow** Accused Products, the "thereby producing a plurality of labeled targets" recited in step (a) occurs when a "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[31] As illustrated below[32], this step produces "a plurality of labelled targets."

[31] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

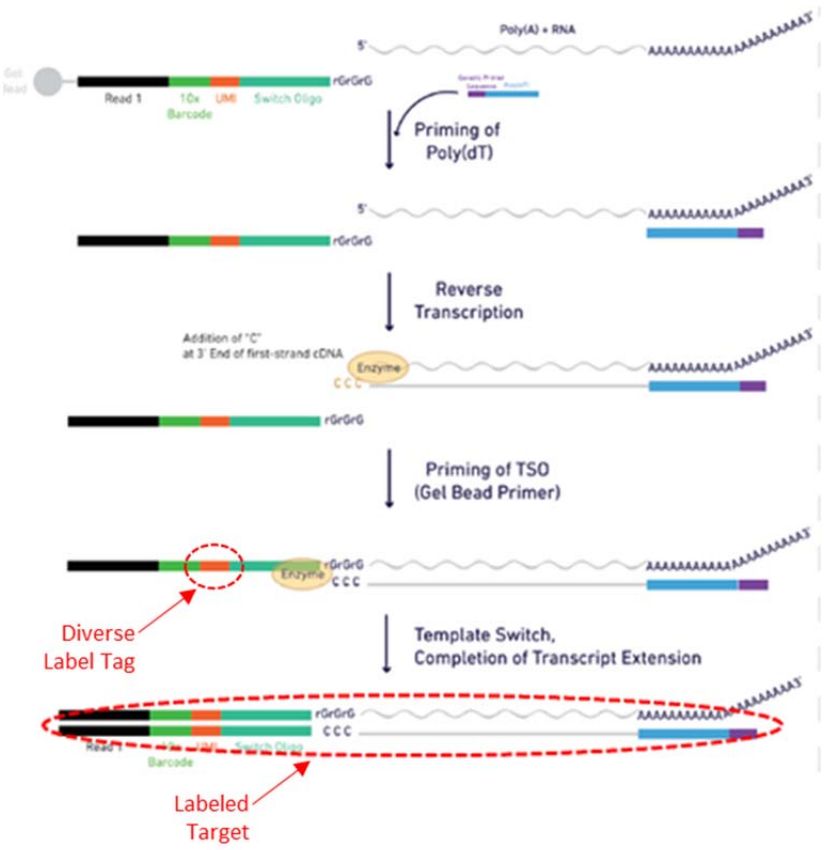
[32] *Id.* at Figure 3 (cropped, markings added)



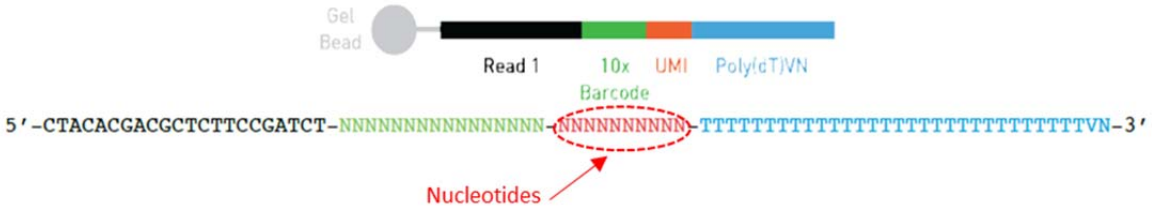
112. In the **Single Cell 5' Workflow** Accused Products, the "thereby producing a plurality of labeled targets" recited in step (a) occurs when "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[33] As illustrated below[34], this step produces "a plurality of labelled targets."

[33] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[34] *Id.* at Figure 3 (cropped, markings added)

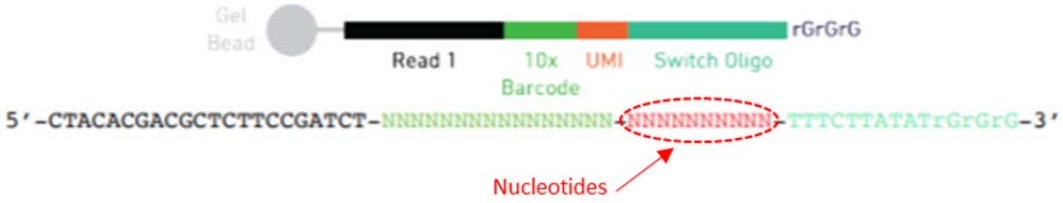


113. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products comprise "a label-tag of the plurality of diverse label-tags comprises nucleotides selected from purine bases, pyrimidine bases, natural nucleotide bases, chemically modified nucleotide bases, biochemically modified nucleotide bases, non-natural nucleotide bases" as recited in substep (i) of step (a). As shown below[35], label tags of the **Single Cell 3' Workflow** Accused Products comprise A, C, G, and T purine bases and pyrimidine bases.



35 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

114. As shown below[36], label tags of the **Single Cell 5' Workflow** Accused Products comprise A, C, G, and T purine bases and pyrimidine bases.



115. As illustrated below[37], in the **Single Cell 3' Workflow** Accused Products, the reverse transcription reaction produces "a labeled target of the plurality of labeled targets" comprising "a distinct label-tag and at least a portion of a nucleic acid target, or its complementary sequence" as recited in substep (ii) of step (a) when "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[38]

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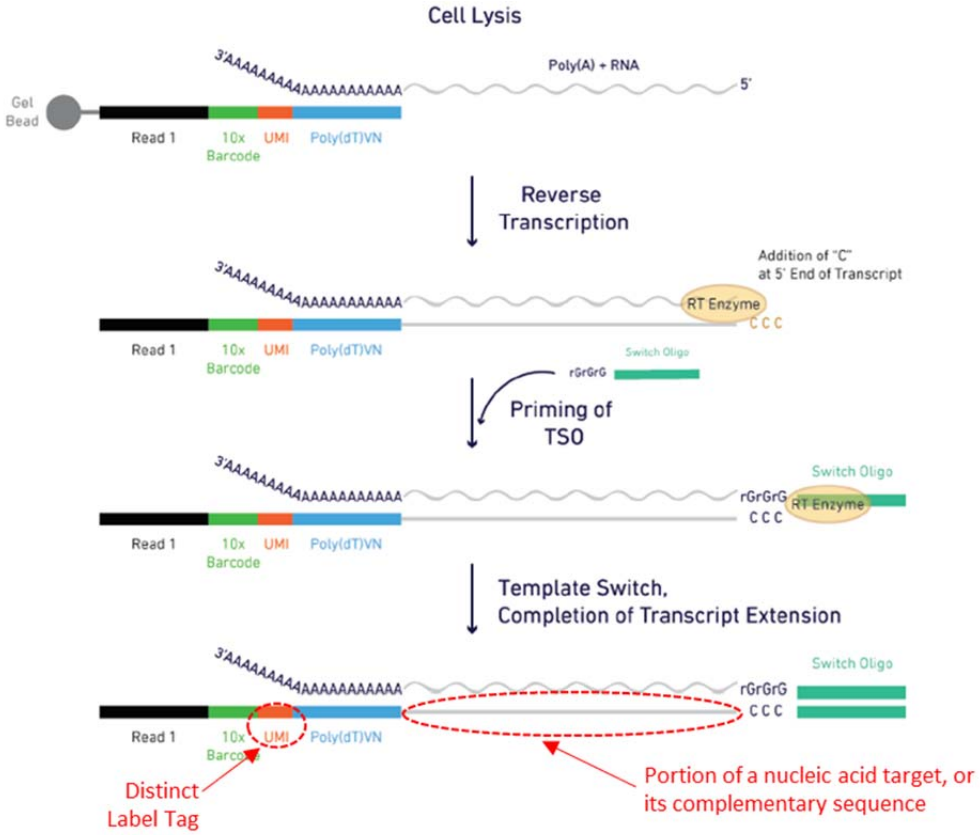
[36] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Table 1 (cropped)

[37] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped, markings added)

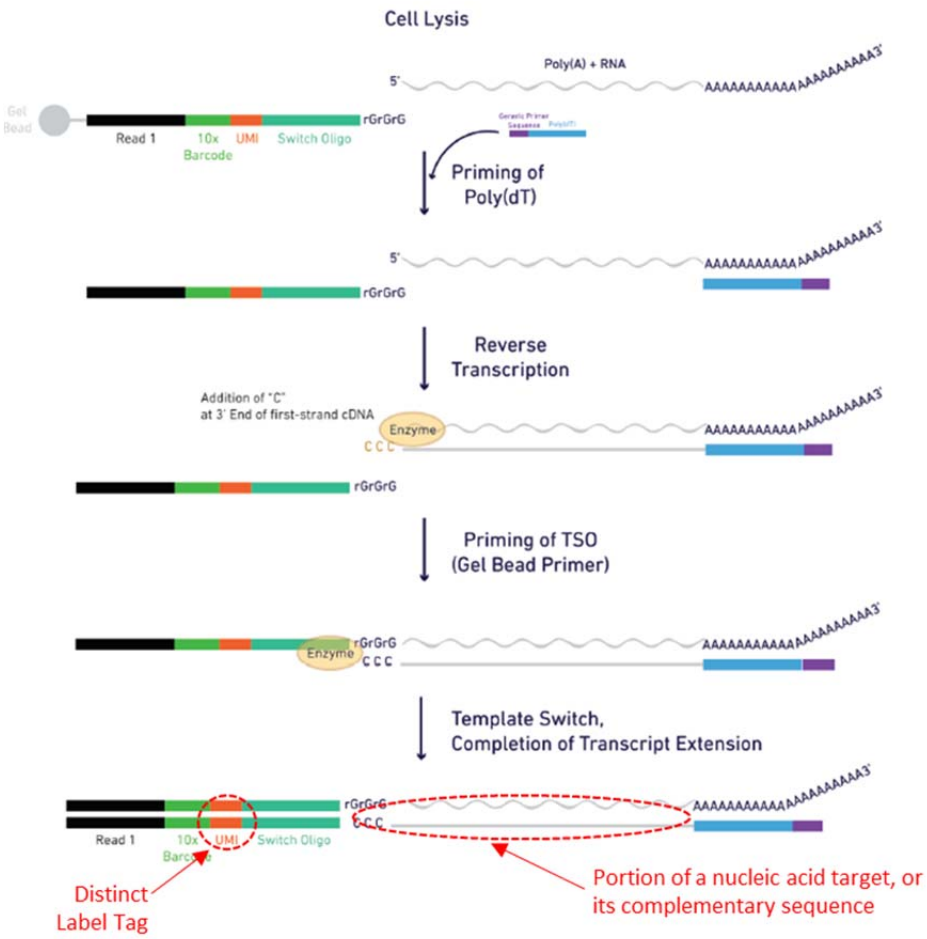
[38] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)



116. As illustrated below[39], in the **Single Cell 5' Workflow** Accused Products, the reverse transcription reaction produces "a labeled target of the plurality of labeled targets" comprising "a distinct label-tag and at least a portion of a nucleic acid target, or its complementary sequence" as recited in substep (ii) of step (a) when "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[40]

[39] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped, markings added)

[40] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

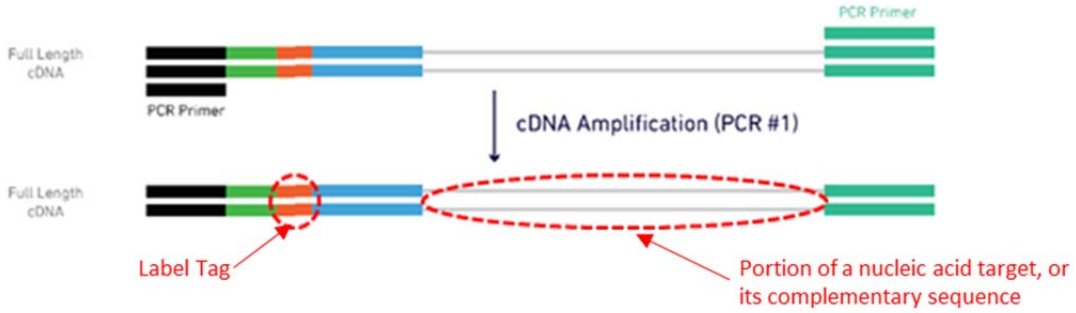


117. In the **Single Cell 3' Workflow** Accused Products, the "amplifying the plurality of labeled-targets to produce a plurality of amplified labeled-targets, wherein an amplified labeled-target of the plurality of amplified labeled-targets comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag" recited in step (b) occurs because "[t]he GEMs are then 'broken', pooling single-stranded, barcoded cDNA molecules from every cell" and "[a] bulk PCR-amplification and Enzymatic Fragmentation" follows.[41] As illustrated below[42], this amplification step results in the "amplified labeled-target of

[41] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

[42] *Id.* at Figure 3 (cropped, markings added)

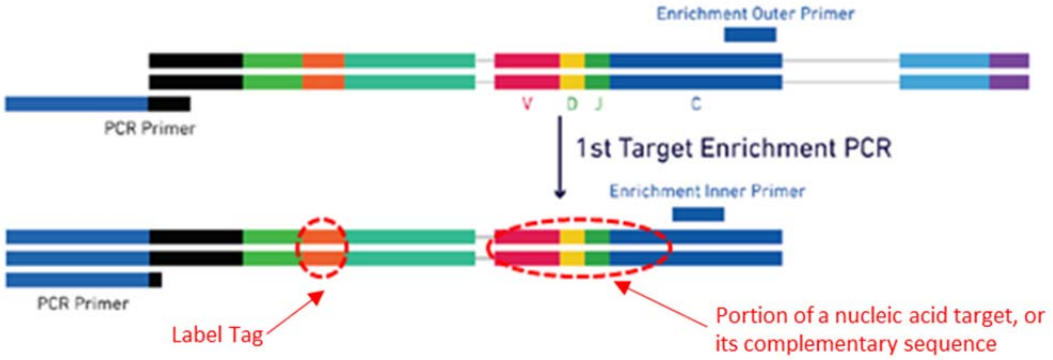
the plurality of amplified labeled-targets" that "comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag."



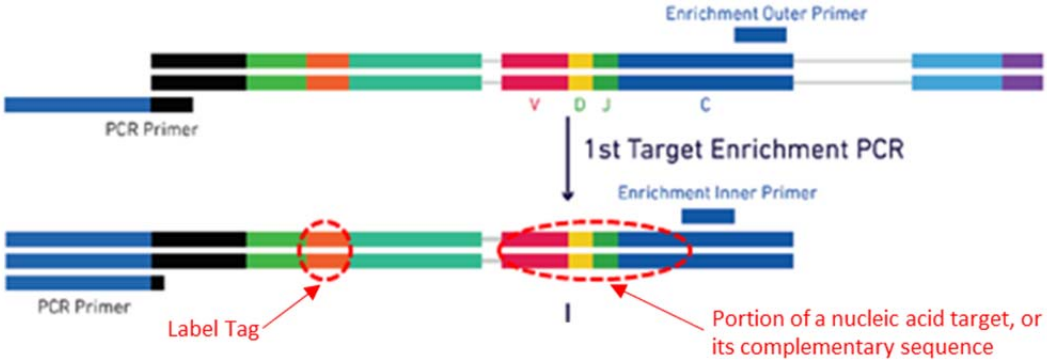
118. In the **Single Cell 5' Workflow** Accused Products, "amplifying the plurality of labeled-targets to produce a plurality of amplified labeled-targets, wherein an amplified labeled-target of the plurality of amplified labeled-targets comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag" recited in step (b) occurs because "[t]he Single Cell V(D)J Solution offers the option to generate" by PCR amplification, "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[43] As illustrated below[44], the Direct Target Enrichment option results in the "amplified labeled-target of the plurality of amplified labeled-targets" that "comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag."

[43] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[44] *Id.* at Figure 3 (cropped, markings added)



119. As illustrated below[45], the cDNA Amplification followed by Target Enrichment option in the **Single Cell 5' Workflow** Accused Products also results in the "amplified labeled-target of the plurality of amplified labeled-targets" that "comprises a copy of at least a portion of the nucleic acid target, or its complementary sequence, and a copy of the label-tag."



120. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, the "detecting the plurality of amplified labeled-targets by sequencing at least a portion of the target and the label-tag" recited in step (c) occurs because "[d]uring library preparation, sequence components essential for Illumina sequencing and downstream data analysis are incorporated into the final library construct,"[46] and because "[t]he Single Cell 3' Protocol produces Illumina-

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45 *Id.* at Figure 4 (cropped, markings added)

46 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

ready sequencing libraries" [47] and "[t]he Single Cell V(D)J Solutions produce V(D)J enriched and 5' gene expression Illumina-ready sequencing libraries."[48] Once these libraries are "generated and sequenced," "the 10x Barcodes are used to associate individual reads back to the individual partitions."[49]

121. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, the "determining the number of copies of the nucleic acid target, as indicated by the number of different label-tags that are associated with the nucleic acid target" recited in step (d) occurs because the amplified products of step (c) are processed with "Cell Ranger™" analysis software to perform "demultiplexing, alignment, and gene counting."[50] The information generated with the Cell Ranger™ software is used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells." [51] "Cell Ranger is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[52] which is "determining the number of copies of the nucleic acid target, as indicated by the number of different label-tags that are associated with the nucleic acid target."

122. 10X has also induced and currently induces infringement of at least claim 1 of the '857 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along

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[47] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf)

[48] "Chromium™ Single Cell V(D)J Reagent Kits User Guide"(CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[49] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[50] *Id.*

[51] *Id.*

[52] https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '857 patent.[53] 10X has known of the '857 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '857 patent.

123. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '857 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '857 patent.[54] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according at least claim 1 of the '857 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '857 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '857 patent. 10X has knowledge of the '857 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '857 patent.

124. Defendant's infringement has been willful and deliberate because Defendant has known of the '857 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '857 patent.

125. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive

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[53] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[54] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages, and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 3
(INFRINGEMENT OF THE '137 PATENT)

126. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

127. U.S. Patent No. 9,816,137 (the "'137 patent"), entitled "Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels," was duly and legally issued on November 14, 2017 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the '137 patent is attached as **Exhibit 3**.

128. The invention of the '137 patent is directed in general to a method of analyzing a sample comprising a plurality of nucleic acids by attaching a plurality of primers to the plurality of nucleic acids from the sample, extending the primers acids to produce a plurality of labeled nucleic acids, and attaching second primers to produce double-stranded labeled nucleic acids

129. Claim 1 of the '137 patent, reproduced below, is representative:

1. A method of analyzing a sample comprising a plurality of nucleic acids, the method comprising:

   a. attaching a plurality of primers to the plurality of nucleic acids from the sample, wherein each primer of the plurality of primers comprises a different variable label region, and the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid;

   b. extending the plurality of primers attached to the plurality of nucleic acids to produce a plurality of labeled nucleic acids, wherein each one of the

plurality of labeled nucleic acids comprises (i) a variable label region; and (ii) a complementary copy of a nucleic acid that was attached to a primer; and

c. attaching a plurality of second primers to the plurality of labeled nucleic acids and extending the plurality of second primers to produce a plurality of double-stranded labeled nucleic acids.

130. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’137 patent, including at least claim 1 of the ’137 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

131. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ’137 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’137 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

132. In the **Single Cell 3’ Workflow** Accused Product “analyzing a sample comprising a plurality of nucleic acids” occurs because “[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell’s transcriptome . . . by partitioning

thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs)" [55] and because cells contain a plurality of poly A-tailed mRNA transcripts,[56] which is a "sample." The "Cell Ranger™" analysis software performs "demultiplexing, alignment, and gene counting"[57] and the information generated with the Cell Ranger software is used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells." [58] "Cell Ranger is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[59] which is "analyzing a sample comprising a plurality of nucleic acids."

133. In the **Single Cell 5' Workflow** Accused Products "analyzing a sample comprising a plurality of nucleic acids" occurs because "[t]he contents of the GEM (oligos, lysed cell components and Master Mix that contains the Poly-dT RT primer) are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA [plurality of nucleic acids] from poly-adenylated mRNA"[60] which is a "sample" and because "Cell Ranger™" analysis software performs "demultiplexing, alignment, and gene counting"[61] and because the information generated with the Cell Ranger software is used for "cell clustering, cell type

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[55] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[56] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf

[57] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf);

[58] *Id.*

[59] https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

[60] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[61] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

classification, and differential gene expression at a scale of hundreds to millions of cells." [62] "Cell Ranger is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[63] which is "analyzing a sample comprising a plurality of nucleic acids."

134. In the **Single Cell 3' Workflow** Accused Products, the "attaching a plurality of primers to the plurality of nucleic acids from the sample, wherein each primer of the plurality of primers comprises a different variable label region, and the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid" of step (a) in claim 1 occurs when "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[64] As illustrated below,[65] "each primer of the plurality of primers comprises a different variable label region." Further, "the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid" because cells contain a plurality of "poly A-tailed mRNA transcripts."[66]

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62 *Id.*

63 https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

64 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

65 *Id.* at Figure 1, Figure 3 (cropped, markings added)

66 *Id.*

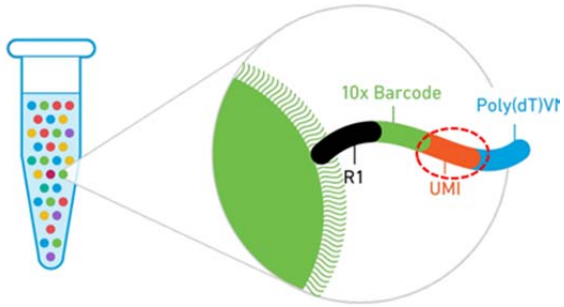
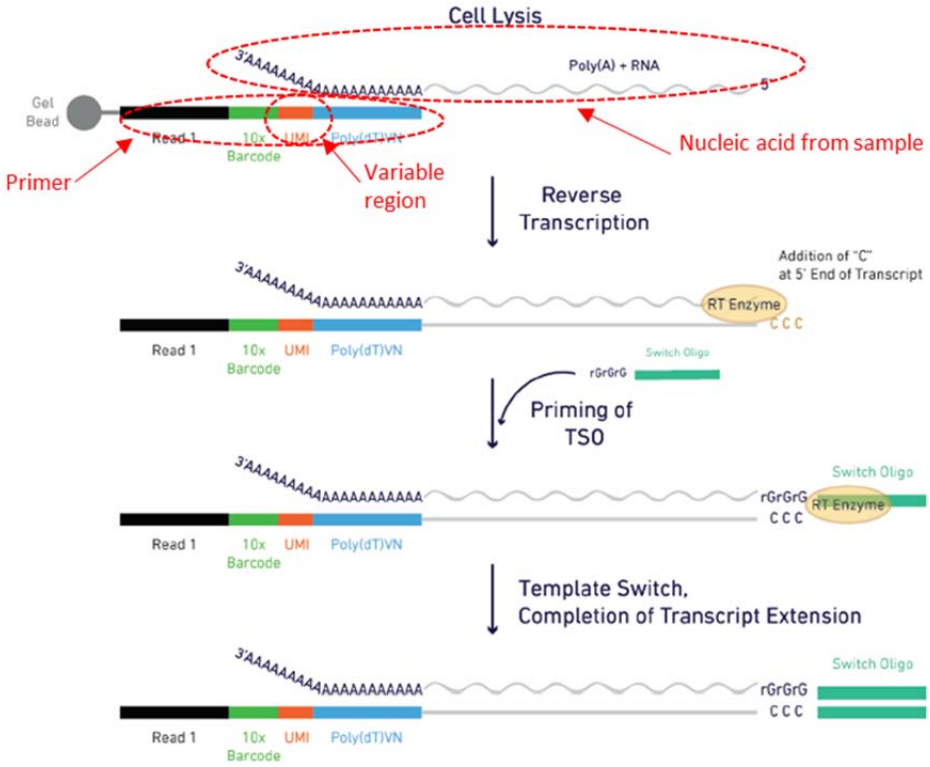


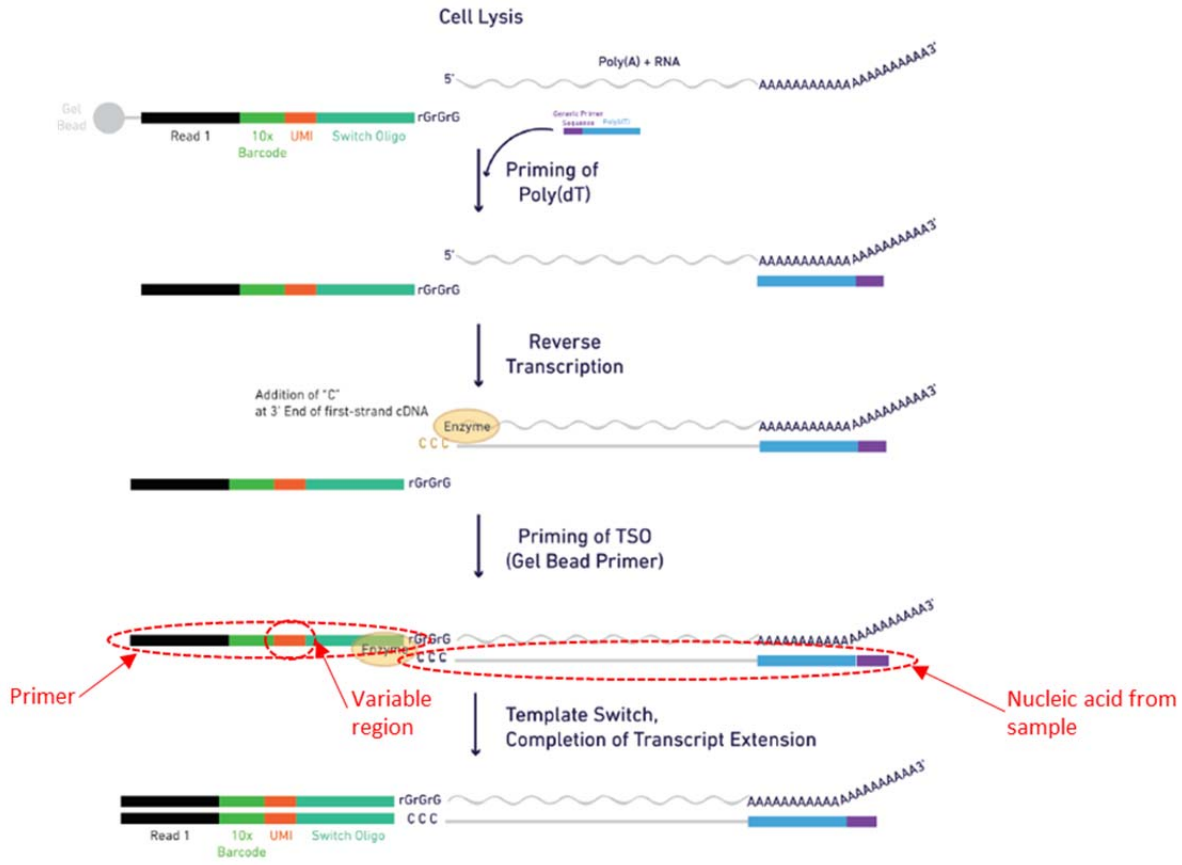
Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.

i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence



135. In the **Single Cell 5' Workflow** Accused Products, the "attaching a plurality of primers to the plurality of nucleic acids from the sample, wherein each primer of the plurality of primers comprises a different variable label region, and the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid" of step (a) in claim 1 occurs when "[t]he contents

of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[67]



136. As illustrated below,[68] "each primer of the plurality of primers comprises a different variable label region" in form of the 10 nucleotide Unique Molecular Identifier (UMI). Further, "the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid" because the reverse transcription products are generated from a plurality of "poly-adenylated mRNA" from the cell[69]

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67 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

68 *Id.* at Figure 1, Figure 3 (cropped, markings added)

69 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

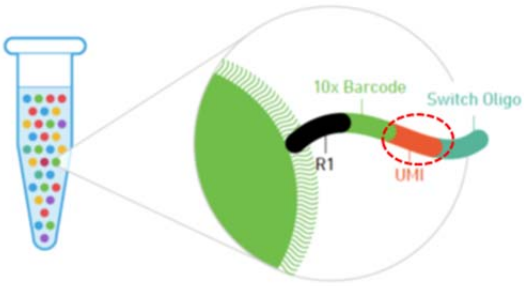


Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

137. As illustrated below,[70] "each primer of the plurality of primers comprises a different variable label region" because each of the beads in both workflows "contain millions of oligo primers" [71] that comprise different "Unique Molecular Identifiers" that make up "a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[72] As shown below[73], these barcodes in the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are a "10nt Unique Molecular Identifier."

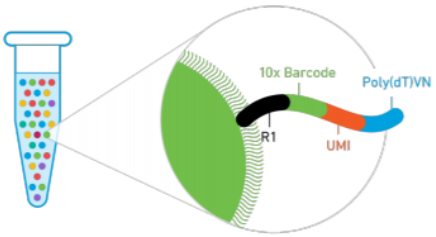
[70] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[71] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[72] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

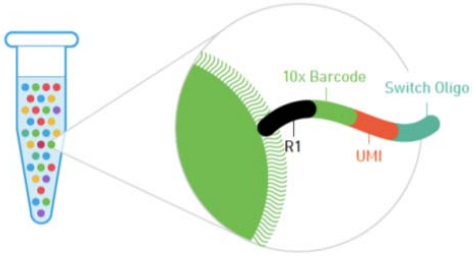
[73] *Id.*

Each Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1):



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

138. Further, in the **Single Cell 3' Workflow** and **Single Cell 5' Workflows,** "the plurality of nucleic acids comprises multiple occurrences of a target nucleic acid" because cells contain a plurality of poly A-tailed mRNA transcripts.[74]

139. In the **Single Cell 3' Workflow** Accused Products, the "extending the plurality of primers attached to the plurality of nucleic acids to produce a plurality of labeled nucleic acids" occurs because a "reverse transcription reaction is primed by the barcoded Gel Bead oligo."[75] As illustrated below[76], the "primers" hybridize to "the plurality of nucleic acids from the sample" and thereby generate the "a plurality of labeled nucleic acids" by an extension reaction wherein

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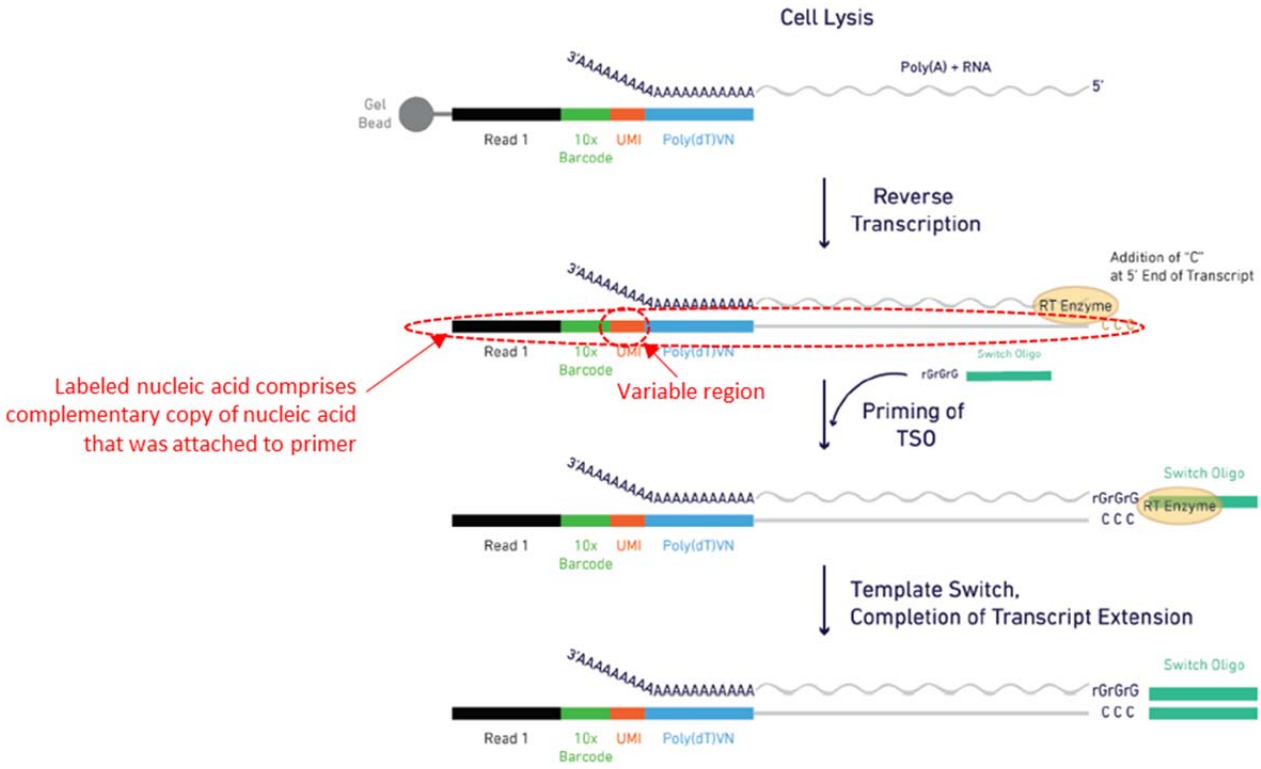
74 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

75 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

76 *Id.* at Figure 3 (cropped, markings added)

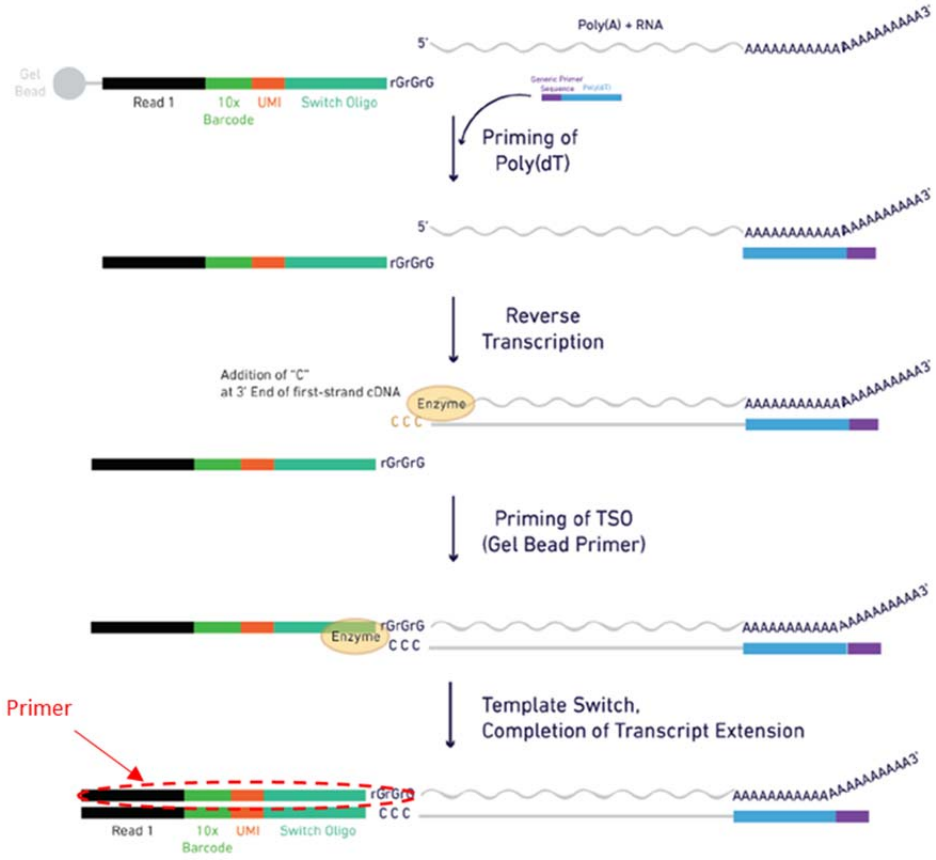
"each one of the plurality of labeled nucleic acids comprises (i) a variable label region; and (ii) a complementary copy of a nucleic acid that was attached to a primer."



140. In the **Single Cell 5' Workflow** Accused Products, the "extending the plurality of primers attached to the plurality of nucleic acids to produce a plurality of labeled nucleic acids wherein each one of the plurality of labeled nucleic acids comprises (i) a variable label region; and (ii) a complementary copy of a nucleic acid that was attached to a primer" occurs because the "Post GEM-RT Cleanup" step uses "DynaBeads MyOne Silane" beads to binds DNA in the sample.[77] On information and belief, "DynaBeads MyOne Silane" bind to DNA fragments at least 50 base pairs in length or larger [78] and therefore will also bind the primer indicated below.

[77] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[78] ThermoFisher Scientific "A complete Workflow for Circulating DNA Isolation and Analysis"



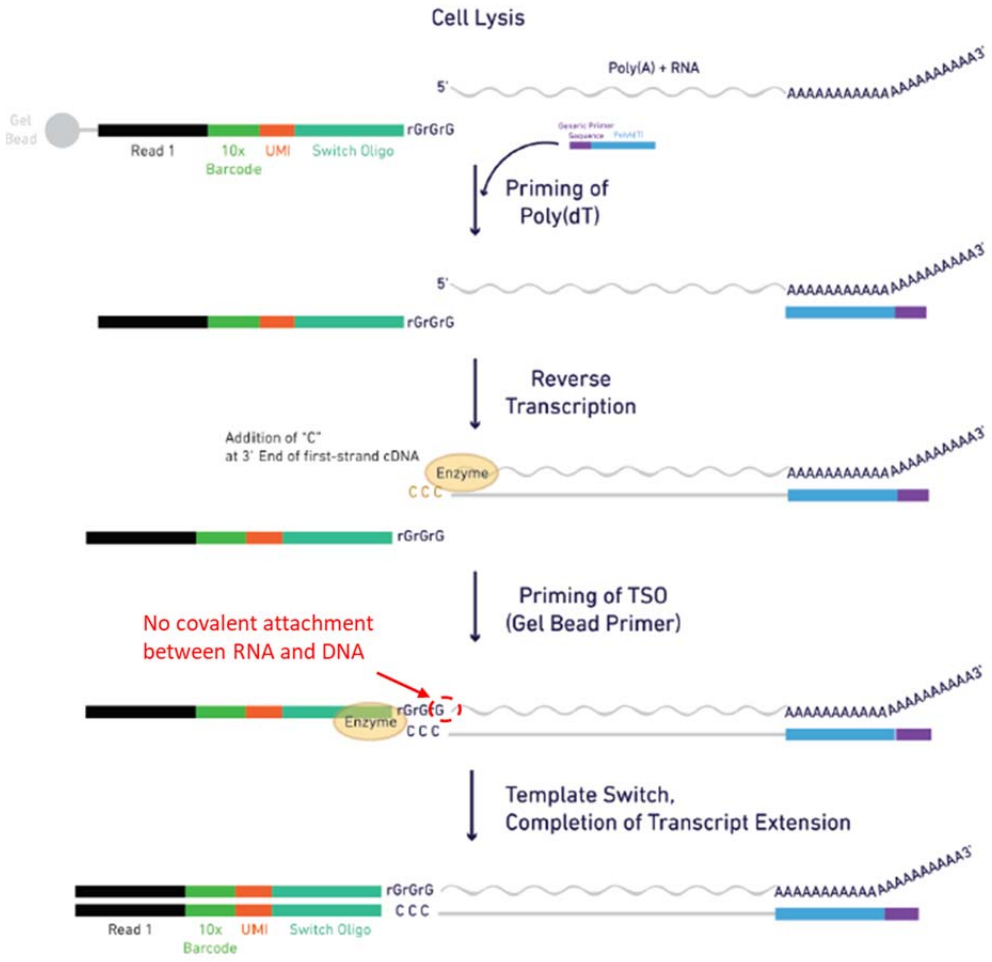
141. The "Post GEM-RT Cleanup" step uses nuclease free water, but does not use ribonuclease-free water. [79] On information and belief, the presence of ribonucleases in the "Post GEM-RT Cleanup Step" will result in degradation of the RNA in the duplex highlighted above to yield the below structure.[80]

142. In the alternative, the **Single Cell 5' Workflow** Accused Products, the "extending the plurality of primers attached to the plurality of nucleic acids to produce a plurality of labeled

[79] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[80] This is illustration is a modification of the figure in the 10x materials adapted to demonstrate the hybrid arising due to the presence of RNAses in the sample.

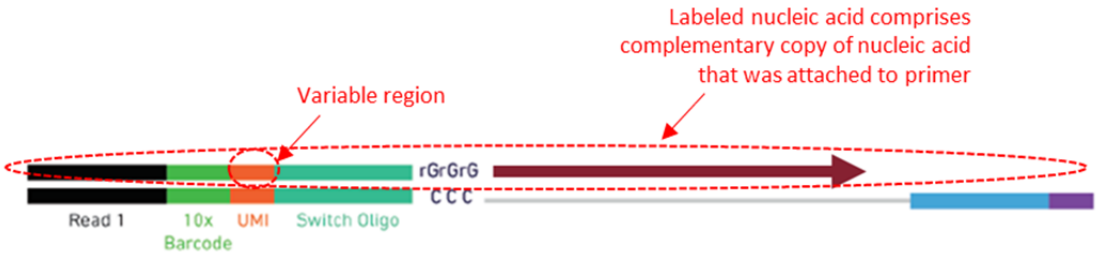
nucleic acids wherein each one of the plurality of labeled nucleic acids comprises (i) a variable label region; and (ii) a complementary copy of a nucleic acid that was attached to a primer" occurs because the RNA molecule in the below illustration is not covalently attached to a DNA molecule.



143. On information and belief, the RNA molecule will dissociate from DNA prior to the PCR amplification step to form the structure illustrated below:[81]

[81] This is illustration is a modification of the figure in the 10x materials adapted to demonstrate the hybrid arising due to dissociation of RNA form the hybrid in the last step of the figure in the preceding paragraph.

144. In the next step of the **Single Cell 5' Workflow** Accused Products, PCR amplification is performed by "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[82] On information and belief, as illustrated with the arrow below, performing either of the PCR extension step will result in "extending the plurality of primers attached to the plurality of nucleic acids to produce a plurality of labeled nucleic acids." As is illustrated below, the extension products generated in this step are a "plurality of labeled nucleic acids [comprising] (i) a variable label region; and (ii) a complementary copy of a nucleic acid that was attached to a primer."



145. In the **Single Cell 3' Workflow** Accused Products, the "attaching a plurality of second primers to the plurality of labeled nucleic acids and extending the plurality of second primers to produce a plurality of double-stranded labeled nucleic acids" occurs because "[t]he GEMs are then 'broken', pooling single-stranded, barcoded cDNA molecules from every cell" and "[a] bulk PCR-amplification and Enzymatic Fragmentation" follows.[83] As illustrated

[82] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[83] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

below[84], in the first step of the reaction, a plurality of PCR primers which are a "plurality of second primers" attach to the plurality of labeled nucleic acids and extend "to produce a plurality of double-stranded labeled nucleic acids."

146. The **Single Cell 5' Workflow** Accused Products "offers the option to generate" by PCR amplification, "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[85] As illustrated below[86], in the Direct Target Enrichment option of the **Single Cell 5' Workflow** Accused Products, the "attaching a plurality of second primers to the plurality of labeled nucleic acids and extending the plurality of second primers to produce a plurality of double-stranded labeled nucleic acids" occurs because "[a]fter incubation, the GEMs are broken and the pooled post GEM-RT reaction mixtures are recovered," followed by "PCR amplification with primers."[87] As illustrated below[88] a plurality of PCR "enrichment outer" primers which are a "plurality of second primers" attach to the plurality of labeled nucleic acids and extend "to produce a plurality of double-stranded labeled nucleic acids."

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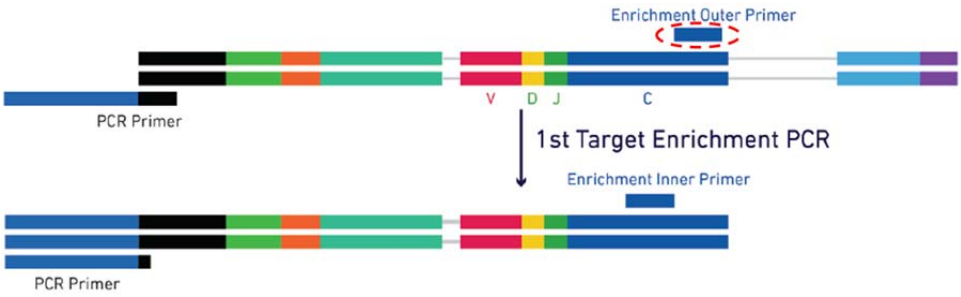
84 *Id.* at Figure 3 (cropped, markings added)

85 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

86 *Id.* at Figure 3 (cropped, markings added)

87 "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

88 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped, markings added)



147. 10X has also induced and currently induces infringement of at least claim 1 of the '137 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '137 patent.[89] 10X has known of the '137 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '137 patent.

148. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '137 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '137 patent.[90] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according at least claim 1 of the '137 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '137 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of

[89] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[90] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

the ’137 patent. 10X has knowledge of the ’137 patent and is aware that the Accused Products are especially made to be used in a system that infringes the ’137 patent.

149. Defendant’s infringement has been willful and deliberate because Defendant has known of the ’137 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the ’137 patent.

150. As the direct and proximate result of Defendant’s conduct, Plaintiffs have suffered and, if Defendant’s conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs’ remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs’ business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 4
(INFRINGEMENT OF THE ’809 PATENT)

151. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

152. U.S. Patent No. 9,290,809 (the “’809 patent”), entitled “Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels,” was duly and legally issued on March 22, 2016 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the ’809 patent is attached as **Exhibit 4**.

153. The invention of the ’809 patent is directed in general to a composition comprising a plurality of oligonucleotide labels, each label comprising an oligo dT sequence, sequencing primer binding site, as well as, a common sequence and a unique label tag.

154. Claim 1 of the ‘809 patent, reproduced below, is representative:

1. A composition comprising a plurality of oligonucleotide labels, wherein each oligonucleotide label of the plurality of oligonucleotide labels comprises

an oligo dT sequence,

a sequencing primer binding site,

a common sequence that is the same for all oligonucleotide labels of the plurality of oligonucleotide labels, and

a unique label tag sequence, wherein the unique label tag sequence is selected from a set of at least m different label tag sequences.

155. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’809 patent, including at least claim 1 of the ’809 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

156. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ‘809 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’809 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

157. Each Gel Bead of the **Single Cell 3' Workflow** Accused Products contains "a plurality of oligonucleotide labels" since the Gel Beads comprise "millions of oligo primers that comprise different Unique Molecular Identifiers" [91] that make up "a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[92] As shown below[93], "each oligonucleotide label of the plurality of oligonucleotide labels" in the **Single Cell 3' Workflow** Accused Products comprise (i) "an oligo dT sequence" ("30nt Poly(dT) primer sequence"), (ii) "a sequencing primer binding site" ("an Illumina® R1 sequence (read 1 sequencing primer)"),[94] (iii) "a common sequence that is the same for all oligonucleotide labels of the plurality of oligonucleotide labels" ("16 nt 10x Barcode")[95], and (iv) "a unique label tag sequence, wherein the unique label tag sequence is selected from a set of at least m different label tag sequences" ("10 nt Unique Molecular Identifier").[96]

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91 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

92 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf)

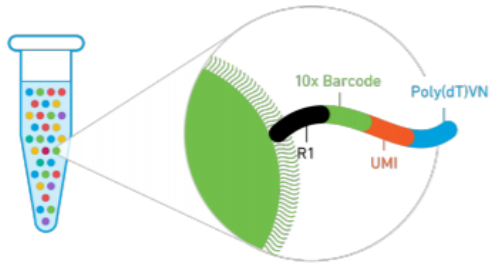
93 *Id.*

94 "During library preparation, sequence components essential for Illumina sequencing and downstream data analysis are incorporated into the final library construct." *See* "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

95 All of the oligonucleotides of a gel bead "share a common 10x Barcode." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

96 "The 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

Each Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1):



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.

158. 10X has also induced and currently induces infringement of at least claim 1 of the '809 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, induces customers to use a composition that infringes at least claim 1 of the '809 patent.[97] 10X has known of the '809 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '809 patent.

159. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '809 patent. 10X has designed the Accused Products specifically to be used with the composition as claimed at least claim 1 of the '809 patent.[98] As such, the Accused Products are a material component of the patented combination, specifically designed for use with the composition of at least claim 1 of the '809 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '809 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not

[97] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[98] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

infringe at least claim 1 of the ’809 patent. 10X i has knowledge of the ’809 patent and is aware that the Accused Products are especially made to be used in a system that infringes the ’809 patent.

160. 10X also has induced and currently induces infringement of at least claim 2 of the ’809 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 2 of the ’809 patent.[99]

161. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 2 of the ’809 patent. 10X has designed the Accused Products specifically to be used in a manner that generates the composition as claimed in at least claim 2 of the ’809 patent.[100] As such, the Accused Products are a material component of the patented combination, specifically designed to make a composition according to at least claim 2 of the ’809 patent, and especially made and adapted for use in a manner that infringes at least claim 2 of the ’809 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 2 of the ’809 patent. 10X has knowledge of the ’809 patent and is aware that the Accused Products are especially made to be used in a system that makes a composition that infringes the ’809 patent.

162. Defendant’s infringement has been willful and deliberate because Defendant has known of the ’809 patent since at least May 2017 and knew or should have known of its

[99] *See, e.g.*, “Chromium™ Single Cell 3’ Reagent Kits v2 User Guide” (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); “Chromium™ Single Cell V(D)J Reagent Kits User Guide” (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[100] *See, e.g.*, “Chromium™ Single Cell 3’ Reagent Kits v2 User Guide” (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); “Chromium™ Single Cell V(D)J Reagent Kits User Guide” (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

infringement but acted despite an objectively high likelihood that such acts would infringe the '809 patent.

163. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 5
(INFRINGEMENT OF THE '808 PATENT)

164. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

165. U.S. Patent No. 9,290,808 (the "'808 patent"), entitled "Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels," was duly and legally issued on March 22, 2016 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the '808 patent is attached as **Exhibit 5**.

166. The invention of the '808 patent is directed in general to a method of determining a number of occurrences of a target molecule from a single cell comprising steps of generating an indexed library by performing a labeling step to thereby generate target-label-tag molecules, amplifying the target-label-tag molecules, and sequencing at least a portion of the target-label-tag molecules.

167. Claim 1 of the '808 patent, reproduced below, is representative:

> 1. A method for determining a number of occurrences of a target molecule from a single cell, the method comprising:

a) generating an indexed library by performing a labeling step, the labeling step comprising:

i) combining in a specified container a sample comprising a plurality of target molecules from the single cell with a plurality of diverse label-tag, wherein the ratio of the number of diverse label-tag sequences to the number of occurrences of a target molecule is greater than 5; and

ii) generating a plurality of target-label-tag molecules by hybridizing label-tags of the plurality of diverse label-tag to target molecules of the plurality of target molecules and performing an extension reaction, wherein a target-label-tag molecule comprises a label-tag and a portion of a complementary sequence of a target molecule;

b) amplifying the target-label-tag molecules from the indexed library; and

c) sequencing at least a portion of the amplified product of step (b) to determine a number of different label-tag sequences associated with the portion of the complementary sequence of a target molecule from the single cell, wherein the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell.

168. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’808 patent, including at least claim 1 of the ’808 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for

sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

169. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the '808 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD's ability to demonstrate Defendant's direct, indirect, literal, or equivalent infringement of additional '808 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

170. As shown below the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are "a method for determining a number of occurrences of a target molecule from a single cell" because the "Cell Ranger™" analysis software performs "demultiplexing, alignment, and gene counting"[101] and because the information generated with the Cell Ranger software is used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells." [102] "Cell Ranger is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[103] which is "determining a number of occurrences of a target molecule from a single cell."

171. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, "generating an indexed library by performing a labeling step" as recited in step (a) of claim 1, wherein the labelling step comprises "combining in a specified container a sample comprising a

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101 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

102 *Id.*

103 https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

plurality of target molecules from the single cell with a plurality of diverse label-tag, wherein the ratio of the number of diverse label-tag sequences to the number of occurrences of a target molecule is greater than 5" as recited in substep (i) of step (a) occurs because "[t]he 10x™ GemCode™ Technology . . . partition[s] thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs),"[104] and/or because "[o]nce partitioned, the Gel Bead dissolves and its oligo primers are released into the aqueous environment of the GEM" [105] and because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome,"[106] and because "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[107]

172. In the **Single Cell 3' Workflow** Accused Products, "generating a plurality of target-label-tag molecules by hybridizing label-tags of the plurality of diverse label-tag to target molecules of the plurality of target molecules and performing an extension reaction, wherein a target-label-tag molecule comprises a label-tag and a portion of a complementary sequence of a target molecule" as recited in substep (ii) of step (a) occurs because a "reverse transcription

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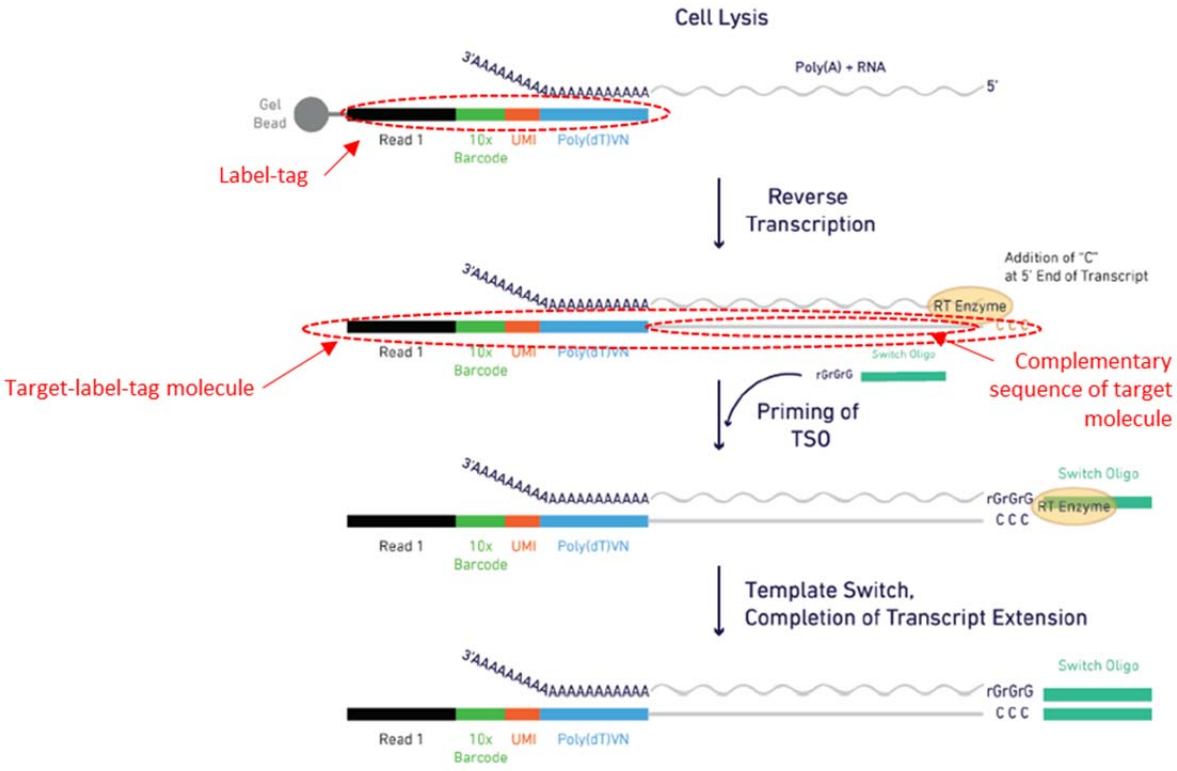
[104] Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[105] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[106] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[107] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); *see also* "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

reaction is primed by the barcoded Gel Bead oligo."[108] As illustrated below[109], the "label-tags of the plurality of diverse label-tag" hybridize to "target molecules of the plurality of target molecules " and thereby generate the "a plurality of target-label-tag molecules " by an extension reaction. Further, as illustrated below[110], the resulting "target-label-tags molecules" comprise "a label-tag and a portion of a complementary sequence of a target molecule" as recited in substep (ii) of step (a).



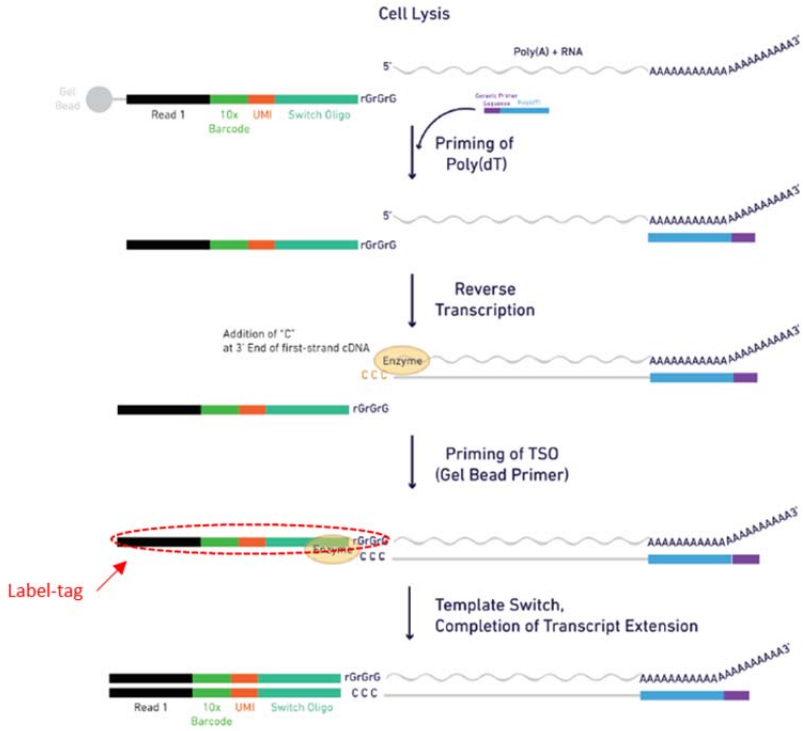
173. In the **Single Cell 5' Workflow** Accused Products, "generating a plurality of target-label-tag molecules by hybridizing label-tags of the plurality of diverse label-tag to target molecules of the plurality of target molecules and performing an extension reaction, wherein a

108 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

109 *Id.* at Figure 3 (cropped, markings added)

110 *Id.*

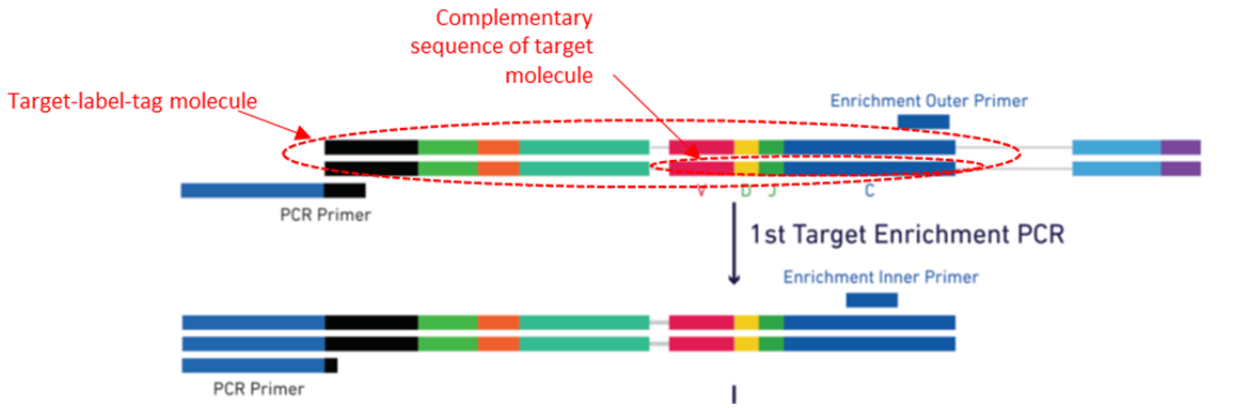
target-label-tag molecule comprises a label-tag and a portion of a complementary sequence of a target molecule" as recited in substep (ii) of step (a) occurs because "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[111] As illustrated below[112], the "label-tags of the plurality of diverse label-tag" hybridize to "target molecules of the plurality of target molecules." The "plurality of target-label-tag molecules" are generated upon a "template switch" and extension in PCR.



174. As illustrated below, the extension step in PCR generates a target-label-tag molecule comprising a label-tag and a portion of a complementary sequence of a target molecule as recited in substep (ii) of step (a).

111 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

112 *Id.* at Figure 3 (cropped, markings added)



175. In the **Single Cell 3' Workflow** Accused Products, the "amplifying the target-label-tag molecules from the indexed library" recited in step (b) of claim 1 occurs because "[t]he GEMs are then 'broken', pooling single-stranded, barcoded cDNA molecules from every cell" and "[a] bulk PCR-amplification and Enzymatic Fragmentation" follows.[113] As illustrated below[114], this PCR step results in amplification of the target-label-tag molecules.

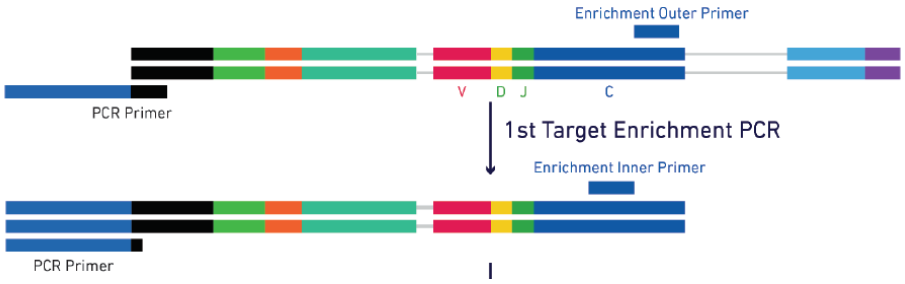
176. In the **Single Cell 5' Workflow** Accused Products, the "amplifying the target-label-tag molecules from the indexed library" recited in step (b) of claim 1 occurs because "[t]he Single Cell V(D)J Solution offers the option to generate" by PCR amplification, "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[115] As illustrated

113 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

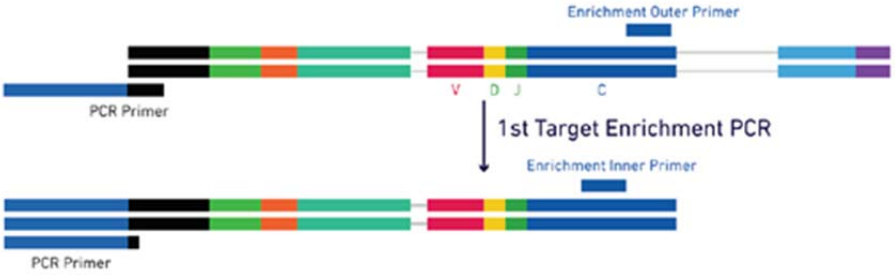
114 *Id.* at Figure 3 (cropped, markings added)

115 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

below[116], the PCR step in "Direct Target Enrichment" option results in amplification of the target-label-tag molecules.



177. As illustrated below[117], the PCR step in "cDNA Amplification followed by Target Enrichment" option also results in amplification of the target-label-tag molecules.



178. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, the "sequencing at least a portion of the amplified product of step (b) to determine a number of different label-tag sequences associated with the portion of the complementary sequence of a target molecule from the single cell" as recited in step (c) of claim 1 occurs because "[d]uring library preparation, sequence components essential for Illumina sequencing and downstream data analysis are incorporated into the final library construct,"[118] and because the Single Cell 3' and Single Cell 5' Workflows produce "Illumina-ready sequencing libraries" and the libraries

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116 *Id.* at Figure 3 (cropped)

117 *Id.* at Figure 4 (cropped)

118 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

"generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions."[119]

179. Further, sequencing in the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products produces a result wherein "the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell" because once these libraries are "generated and sequenced," "the 10x Barcodes are used to associate individual reads back to the individual partitions."[120] Correlation between "the number of different label-tag sequences" and "the number of occurrences of the target molecule from the single cell" as recited in step (c) occurs because the amplified products of step (b) of claim 1 are processed with "Cell Ranger™" analysis software to perform "demultiplexing, alignment, and gene counting."[121] The information generated with the Cell Ranger™ software can be used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells."[122] "Cell Ranger™ is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[123] which is a sub-element wherein "the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell."

180. 10X has also induced and currently induces infringement of at least claim 1 of the '808 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along

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119 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

120 *Id.*

121 *Id.*

122 *Id.*

123 https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '808 patent.[124] 10X has known of the '808 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '808 patent.

181. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '808 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '808 patent.[125] As such, the accused products are a material component of the patented combination, specifically designed to be used according to at least claim 1 of the '808 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '808 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '808 patent. 10X has knowledge of the '808 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '808 patent.

182. Defendant's infringement has been willful and deliberate because Defendant has known of the '808 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '808 patent.

183. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive

[124] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[125] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 6
(INFRINGEMENT OF THE '659 PATENT)

184. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

185. U.S. Patent No. 9,708,659 (the "'659 patent"), entitled "Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels," was duly and legally issued on July 18, 2017 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the '659 patent is attached as **Exhibit 6**.

186. The invention of the '659 patent is directed in general to a system for counting a number of nucleic acid target molecules that are present in a single cell. The system comprises five times more different labels (from a set of diverse labels), as compared to the number of nucleic acid target molecules. The system further comprises reaction vessels for attaching the different labels to the nucleic acid target molecules and processing software for counting the number of nucleic acid target molecules from a number of labeled nucleic acid target molecules detected.

187. Claim 1 of the '659 patent, reproduced below, is representative:

> 1. A system for counting n, wherein n is a number of nucleic acid target molecules that are present in a single cell from a sample comprising cells, the system comprising:
>
> a) a diverse set of labels, wherein the set comprises m different labels, wherein the ratio of m to n is greater than 5;

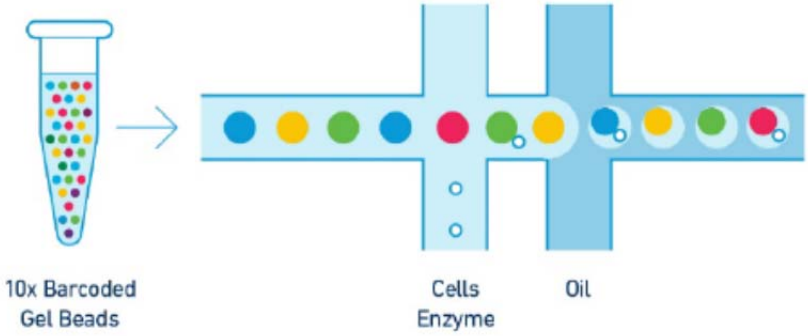
b) a plurality of reaction vessels for attaching a label from the diverse set of labels to each occurrence of the nucleic acid target molecules from each single cell from said sample comprising cells to generate a set of labeled nucleic acid target molecules, wherein the individual labeled nucleic acid target molecules comprise all or a portion of the complementary sequence of a nucleic acid target molecule and a label from the diverse set of labels; and

c) processing software for counting n from a number of labeled nucleic acid target molecules detected.

188. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’659 patent, including at least claim 1 of the ’659 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

189. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ‘659 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’659 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

190. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are "a system for counting n, wherein n is a number of nucleic acid target molecules that are present in a single cell from a sample comprising cells" as recited in claim 1, because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome . . . by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs)." [126] As illustrated below,[127] "the cells are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs contains no cell, while the remainder largely contain a single cell."



191. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are for "counting n, wherein n is a number of nucleic acid target molecules" because the "Cell Ranger™" analysis software performs "demultiplexing, alignment, and gene counting"[128] and because the information generated with the Cell Ranger software is used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells."[129] "Cell Ranger is a set of analysis pipelines [that perform gene expression analysis by] alignment,

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126 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

127 *Id.*

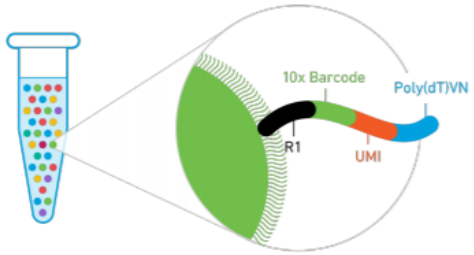
128 *Id.*

129 *Id.*

filtering, barcode counting, and UMI counting,"[130] which is "counting n, wherein n is a number of nucleic acid target molecules system produces."

192. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products comprise "a diverse set of labels, wherein the set comprises m different labels" because "Gel Beads are… functionalized with millions of copies of a 10x Barcoded primer."[131] As illustrated below[132], the system comprises "~ 750000 barcodes to separately index each cell's transcriptome." [133] As shown below[134], the "diverse set of labels, wherein the set comprises m different labels" in the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products is the "10nt Unique Molecular Identifier."

Each Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1):



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.

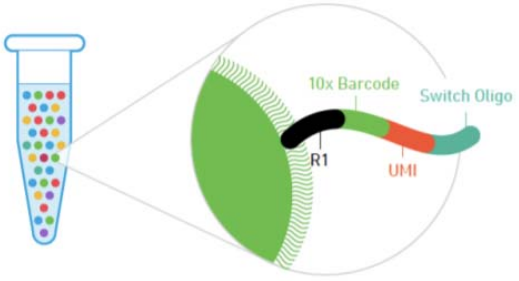
130 https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

131 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

132 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

133 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

134 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

193. In the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products, "the ratio of m to n is greater than 5" as recited in step (a) because "[t]he 10x™ GemCode™ Technology… samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome" [135] and because the "number of nucleic acid target molecules that are present in a single cell" is less than 150000. For example, single cell analysis shows "~4,500 genes and 27,000 transcripts […] detected" human and mouse cells.[136]

194. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products comprise "a plurality of reaction vessels for attaching a label from the diverse set of labels to each occurrence of the nucleic acid target molecules from each single cell from said sample comprising cells" as recited in step (b) of claim 1 because "[t]he 10x™ GemCode™ Technology… partition[s] thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs),"[137] and because "[o]nce partitioned, the Gel Bead dissolves and its oligo primers are

[135] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide": CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf

[136] "Chromium™ Single Cell Solutions 10x Single Cell App Note" (10x_Single_Cell_App_Note.pdf)

[137] Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

released into the aqueous environment of the GEM" [138] and because "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[139]

195. The **Single Cell 3' Workflow** Accused Products comprise "a plurality of reaction vessels for attaching a label from the diverse set of labels to each occurrence of the nucleic acid target molecules from each single cell from said sample comprising cells to generate a set of labeled nucleic acid target molecules" as recited in step (b) of claim 1 because a "reverse transcription reaction is primed by the barcoded Gel Bead oligo."[140] As illustrated below[141], the "labels" are attached to "nucleic acid target molecules from each single cell" and thereby generate the "set of labeled nucleic acid target molecules" by an extension reaction, which "comprise all or a portion of the complementary sequence of a nucleic acid target molecule and a label from the diverse set of labels" as recited in step (b) of claim 1.

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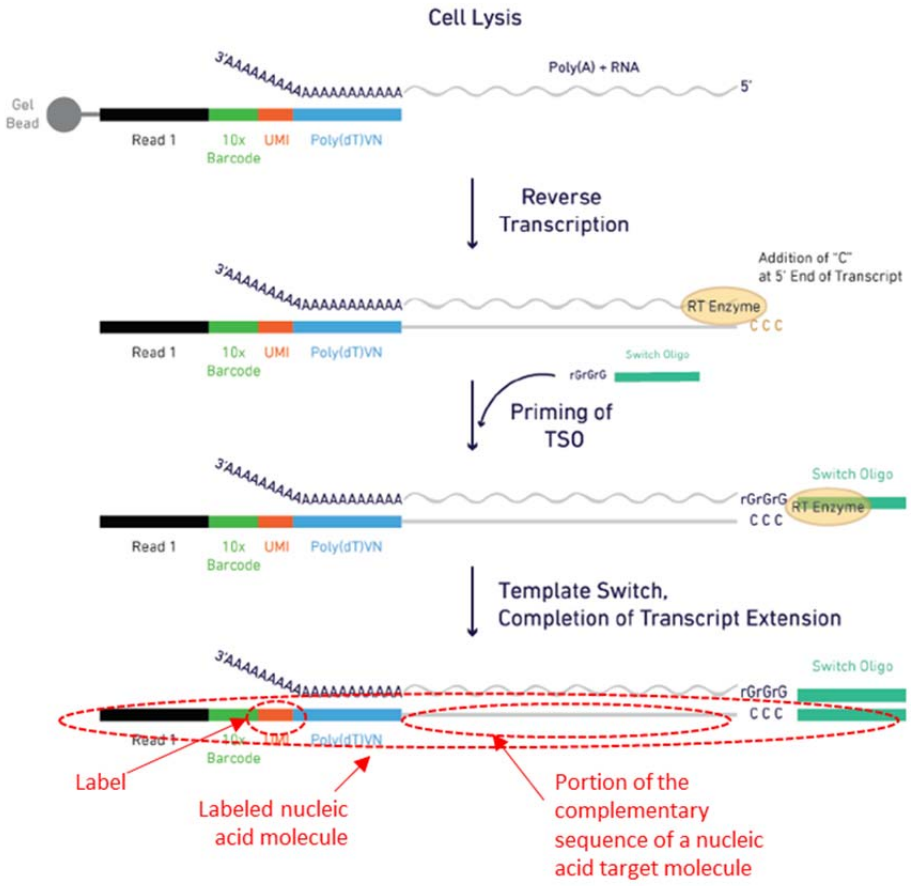
138 TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

139 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); *see also* "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.docx)

140 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

141 *Id.* at Figure 3 (cropped, markings added)

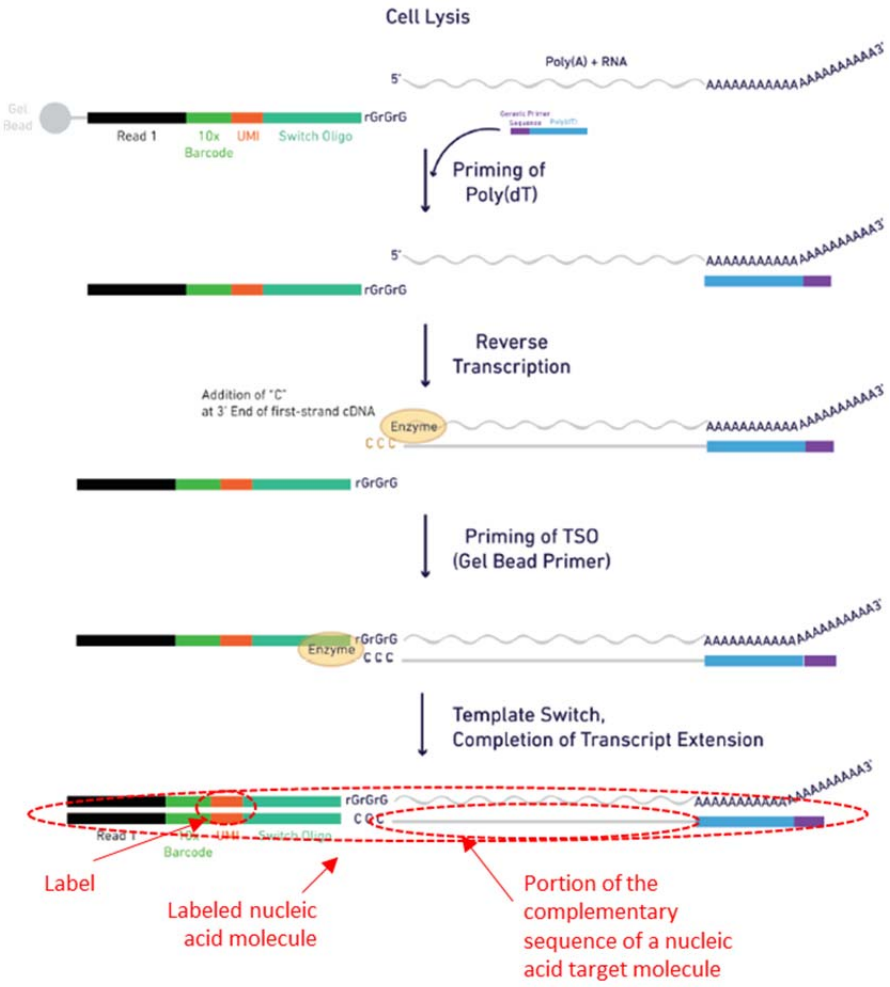


196. The **Single Cell 5' Workflow** Accused Products comprise "a plurality of reaction vessels for attaching a label from the diverse set of labels to each occurrence of the nucleic acid target molecules from each single cell from said sample comprising cells to generate a set of labeled nucleic acid target molecules" as recited in step (a) of claim 1 because "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[142] As illustrated below[143], the "labels" hybridize to a reverse transcription product of the "nucleic acid target molecules." The "set of labeled nucleic acid target molecules" are generated upon a "template switch" step, each of

142 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

143 *Id.* at Figure 3 (cropped, markings added)

which "comprise all or a portion of the complementary sequence of a nucleic acid target molecule and a label from the diverse set of labels" as recited in step (b) of claim 1.



197. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products comprise "processing software for counting n from a number of labeled nucleic acid target molecules detected" as recited in step (c) of claim 1 because "the 10x Barcodes are used to associate individual reads back to the individual partitions[144] using "Cell Ranger™" analysis

[144] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

software to perform "demultiplexing, alignment, and gene counting."[145] The information generated with the Cell Ranger software is used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells."[146]

198. 10X has also induced and currently induces infringement of at least claim 1 of the '659 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '659 patent.[147] 10X has known of the '659 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '659 patent.

199. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '659 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '659 patent.[148] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according to at least claim 1 of the '659 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '659 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of

145 *Id.*

146 *Id.*

147 *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

148 *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

the ’659 patent. 10X has knowledge of the ’659 patent and is aware that the Accused Products are especially made to be used in a system that infringes the ’659 patent.

200. Defendant’s infringement has been willful and deliberate because Defendant has known of the ’659 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the ’659 patent.

201. As the direct and proximate result of Defendant’s conduct, Plaintiffs have suffered and, if Defendant’s conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs’ remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs’ business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 7
(INFRINGEMENT OF THE ’502 PATENT)

202. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

203. U.S. Patent No. 9,845,502 (the “’502 patent”), entitled “Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels,” was duly and legally issued on December 19, 2017 to inventors Stephen P. A. Fodor and Glenn K. Fu. A true and accurate copy of the ’502 patent is attached as **Exhibit 7**.

204. The invention of the ’502 patent is directed in general to a method for determining a number of occurrences of a target molecule from a single cell, the method comprising steps of generating an indexed library comprising a plurality of target-label-tag molecules by performing a labeling step, amplifying the plurality of target-label-tag molecules to generate amplified products, and sequencing at least a portion of the plurality of amplified products.

205. Claim 1 of the ’502 patent, reproduced below, is representative:

1. A method for determining a number of occurrences of a target molecule from a single cell, the method comprising:

a) generating an indexed library by performing a labeling step, the labeling step comprising:

i) combining each of a target molecule from a plurality of target molecules from a single cell with a label-tag from a plurality of diverse label-tags, wherein the ratio of the number of the plurality of diverse label-tags to the number of each of the plurality of target molecules is greater than 5; and

ii) generating the indexed library comprising a plurality of target-label-tag molecules by hybridizing the label-tag of the plurality of diverse label-tags to the target molecule of the plurality of target molecules and performing an extension reaction, wherein a target-label-tag molecule comprises the label-tag and a portion of a complementary sequence of the target molecule;

b) amplifying the plurality of target-label-tag molecules from the indexed library to generate a plurality of amplified products; and

c) sequencing at least a portion of the plurality of amplified products of step (b) to determine a number of different label-tag sequences associated with the portion of the complementary sequence of the target molecule from the single cell, wherein the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell.

206. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’502 patent, including at least claim 1 of the ’502 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

207. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ‘502 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’502 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

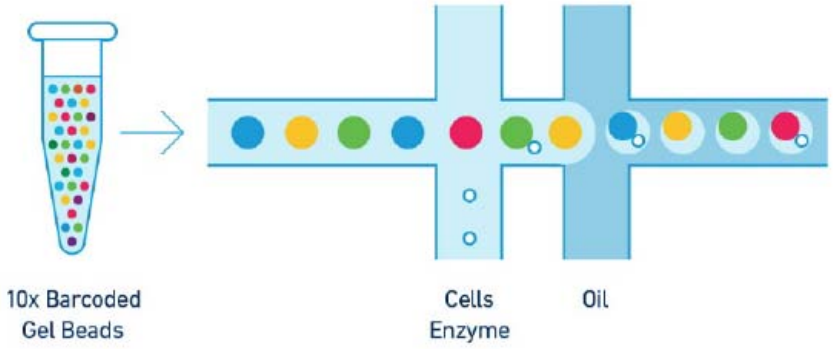
208. The **Single Cell 3’ Workflow** and **Single Cell 5’ Workflow** Accused Products are “a method for determining a number of occurrences of a target molecule from a single cell” as recited in claim 1, because the “Cell Ranger™” analysis software performs “demultiplexing, alignment, and gene counting”[149] and the information generated with the Cell Ranger™ [150] software is used for “cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells.”[151] Cell Ranger™ is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,”

[149] “Chromium™ Single Cell 3’ Reagent Kits v2 User Guide” (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); “Chromium™ Single Cell V(D)J Reagent Kits User Guide” (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[150] *Id.*

[151] *Id.*

which is "determining a number of occurrences of a target molecule from a single cell."[152] "The 10x™ GemCode™ Technology partition[s] thousands of cells" with the 10x Barcoded Gel Beads "into nanoliter-scale Gel Bead-In-EMulsions (GEMs)."[153] As illustrated below[154], "the cells are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs contains no cell, while the remainder largely contain a single cell."[155]



209. In the **Single Cell 3' Workflow** Accused Products "generating an indexed library by performing a labeling step, the label step comprising (i) combining each of a target molecule from a plurality of target molecules from a single cell with a label-tag from a plurality of diverse label-tags" as recited in step (a) and substep (a)(i) of claim 1 occurs because a "[t]he contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[156] In the **Single Cell 3' Workflow** Accused Products, "the ratio of the number of the plurality of diverse

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152 https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

153 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

154 *Id.*

155 *Id.*

156 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

label-tags to the number of each of the plurality of target molecules is greater than 5" as recited in step (a) and substep (a)(i) of claim 1 because "[t]he 10x™ GemCode™ Technology… samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome" [157] and because the "number of each of the plurality of target molecules" is less than 150000. For example, single cell analysis shows "~4,500 genes and 27,000 transcripts […] detected" human and mouse cells.[158]

210. In the **Single Cell 3' Workflow** Accused Products, "generating the indexed library comprising a plurality of target-label-tag molecules by hybridizing the label-tag of the plurality of diverse label-tags to the target molecule of the plurality of target molecules and performing an extension reaction" as recited in claim 1 step (a) substep (ii) occurs because a "reverse transcription reaction is primed by the barcoded Gel Bead oligo."[159] As illustrated below[160], the "label-tag of the plurality of diverse label tags" hybridize to "the target molecule of the plurality of target molecules" and thereby generate the "target-label-tag molecules" by an extension reaction. Further, as illustrated below[161], the resulting "target-label-tag molecules" comprise "the label-tag and a portion of a complementary sequence of the target molecule" as recited in substep (ii) of step (a).

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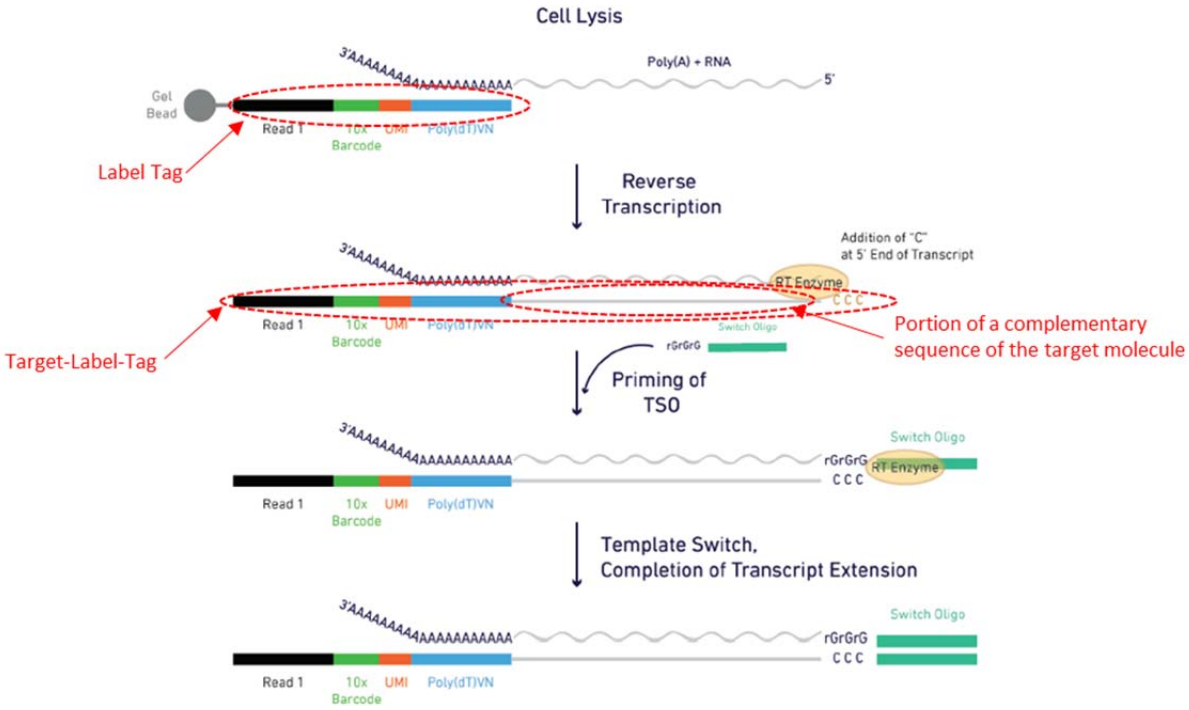
157 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

158 Chromium™ Single Cell Solutions 10x Single Cell App Note (10x_Single_Cell_App_Note.pdf)

159 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

160 *Id.* at Figure 3 (cropped, markings added)

161 *Id.*



211. In the **Single Cell 5' Workflow** Accused Products, "generating an indexed library by performing a labeling step, the label step comprising combining each of a target molecule from a plurality of target molecules from a single cell with a label-tag from a plurality of diverse label-tags" as recited in step (a) and substep (a)(i) of claim 1 because "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[162] In the **Single Cell 5' Workflow** Accused Products, "the ratio of the number of the plurality of diverse label-tags to the number of each of the plurality of target molecules is greater than 5" as recited in step (a) and substep (a)(i) of claim 1 because "[t]he 10x™ GemCode™ Technology… samples a pool of ~ 750000 barcodes to separately

[162] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

index each cell's transcriptome" [163] and because the "number of each of the plurality of target molecules" is less than 150000. For example, single cell analysis shows "~4,500 genes and 27,000 transcripts […] detected" human and mouse cells.[164]

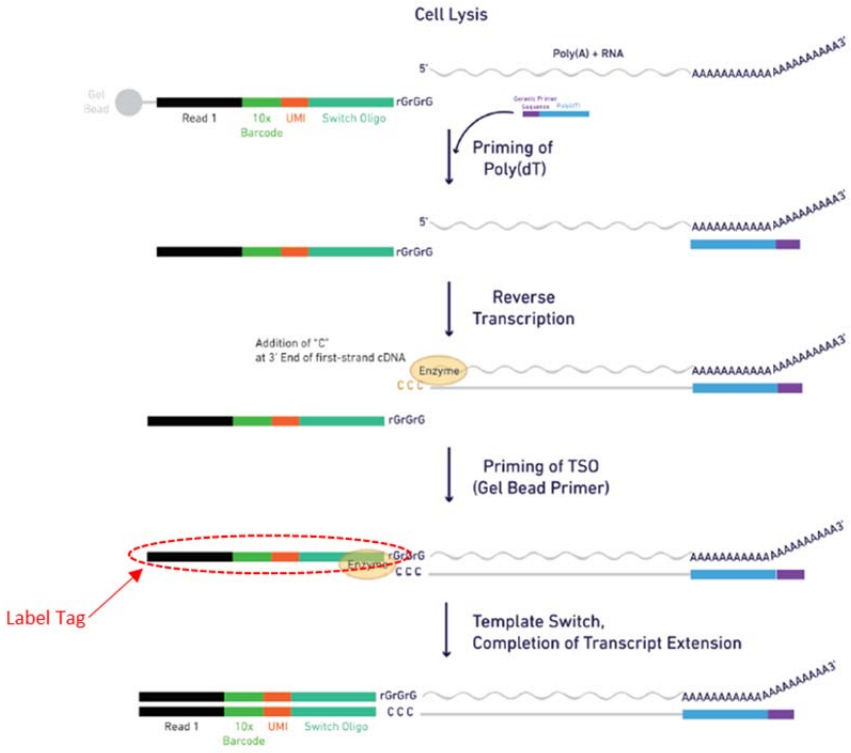
212. In the **Single Cell 5' Workflow** Accused Products, "generating the indexed library comprising a plurality of target-label-tag molecules by hybridizing the label-tag of the plurality of diverse label-tags to the target molecule of the plurality of target molecules and performing an extension reaction" as recited in claim 1 step (a) substep (ii) occurs because "[t]he contents of the GEM […] are incubated in a reverse transcription (RT) reaction to generate full-length, barcoded cDNA from poly-adenylated mRNA."[165] As illustrated below[166], the "label-tag of the plurality of diverse label tags" hybridize to a reverse transcription product which is the "target molecule."

[163] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[164] Chromium™ Single Cell Solutions 10x Single Cell App Note (10x_Single_Cell_App_Note.pdf)

[165] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[166] *Id.* at Figure 3 (cropped, markings added)



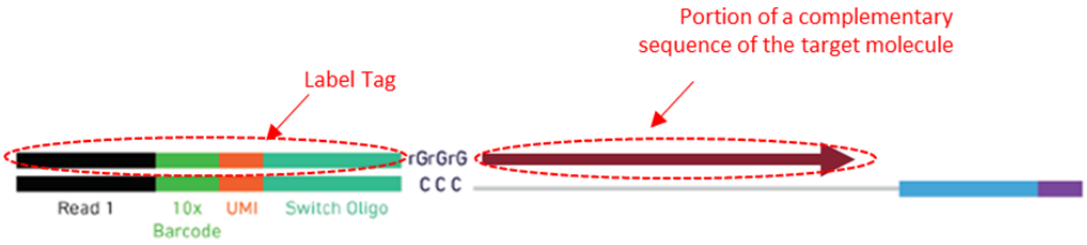
213. On information and belief, the RNA molecule will dissociate from DNA prior to the PCR amplification step to form the structure illustrated below:[167]

214. In the next step of the **Single Cell 5' Workflow** Accused Products, PCR amplification is performed by "Direct Target Enrichment" or "cDNA Amplification followed by Target Enrichment."[168] On information and belief, as illustrated with the arrow below, performing either of the PCR extension step will result in "performing an extension reaction, wherein a target-label-tag molecule comprises the label-tag and a portion of a complementary

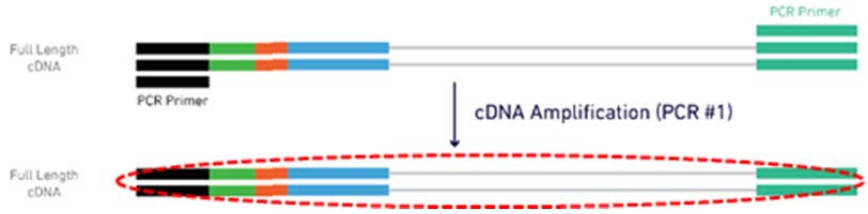
[167] This is illustration is a modification of the figure in the 10x materials adapted to demonstrate the hybrid arising due to dissociation of RNA form the hybrid in the last step of the figure in the preceding paragraph.

[168] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

sequence of the target molecule." As is illustrated below, the extension products generated in this step are a "a target-label-tag molecule [comprising] the label-tag and a portion of a complementary sequence of the target molecule."



215. The **Single Cell 3' Workflow** Accused Products comprise a step of "amplifying the plurality of target-label-tag molecules from the indexed library to generate a plurality of amplified products" as recited in step (b) of claim 1 because "[t]he GEMs are then 'broken', pooling single-stranded, barcoded cDNA molecules from every cell" and "[a] bulk PCR-amplification and Enzymatic Fragmentation" follows.[169] As illustrated below[170], this PCR step results in amplification of the target-label-tag molecules.

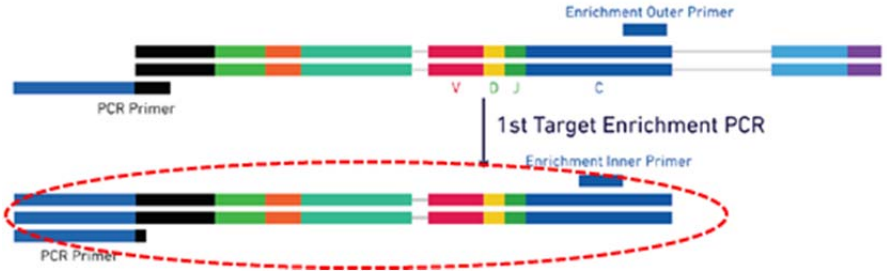


216. In the **Single Cell 5' Workflow** Accused Products, the "amplifying the plurality of target-label-tag molecules from the indexed library to generate a plurality of amplified products" recited in step (b) of claim 1 occurs because "[t]he Single Cell V(D)J Solution offers the option to generate" by PCR amplification, "Direct Target Enrichment" or "cDNA

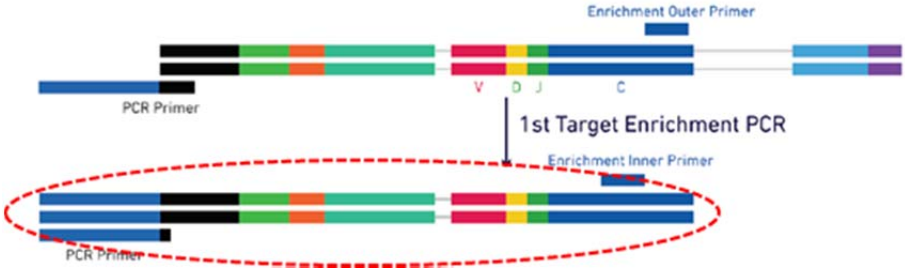
169 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

170 *Id.* at Figure 3 (cropped, markings added)

Amplification followed by Target Enrichment."[171] As illustrated below[172], the PCR step in "Direct Target Enrichment" option results in amplification of the target-label-tag molecules.



217. As illustrated below[173], the PCR step in "cDNA Amplification followed by Target Enrichment" option also results in amplification of the target-label-tag molecules.



218. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products comprise a step of "sequencing at least a portion of the plurality of amplified products of step (b) to determine a number of different label-tag sequences associated with the portion of the complementary sequence of the target molecule from the single cell" as recited in step (c) of claim 1 because "[d]uring library preparation, sequence components essential for Illumina

171 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

172 *Id.* at Figure 3 (cropped, markings added)

173 *Id.* at Figure 4 (cropped, markings added)

sequencing and downstream data analysis are incorporated into the final library construct,"[174] and because the Single Cell 3' and Single Cell 5' Workflows produce "Illumina-ready sequencing libraries" and the libraries "generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions."[175]

219. Further, sequencing in the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products produces a result "wherein the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell" because once these libraries are "generated and sequenced," "the 10x Barcodes are used to associate individual reads back to the individual partitions."[176] Correlation between the "the number of different label-tag sequences" and "the number of occurrences of the target molecule from the single cell" as recited in step (c) occurs because the amplified products of step (b) of claim 1 are processed with "Cell Ranger™" analysis software to perform "demultiplexing, alignment, and gene counting."[177] The information generated with the Cell Ranger software can be used for "cell clustering, cell type classification, and differential gene expression at a scale of hundreds to millions of cells."[178] "Cell Ranger™ is a set of analysis pipelines [that perform gene expression analysis by] alignment, filtering, barcode counting, and UMI counting,"[179] which is a

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174 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

175 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

176 *Id.*

177 *Id.*

178 *Id.*

sub-element "wherein the number of different label-tag sequences indicates the number of occurrences of the target molecule from the single cell."

220. 10X has also induced and currently induces infringement of at least claim 1 of the '502 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '502 patent.[180] 10X has known of the '502 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '502 patent.

221. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '502 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '502 patent.[181] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according to at least claim 1 of the '502 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '502 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '502 patent. 10X has knowledge of the '502 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '502 patent.

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[179] https://support.10xgenomics.com/single-cell-gene-expression/software/pipelines/latest/what-is-cell-ranger

[180] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[181] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

222. Defendant's infringement has been willful and deliberate because Defendant has known of the '502 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '502 patent.

223. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 8
(INFRINGEMENT OF THE '645 PATENT)

224. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

225. U.S. Patent No. 9,567,645 (the "'645 patent"), entitled "Massively Parallel Single Cell Analysis," was duly and legally issued on February 14, 2017 to inventors Christina Fan, Stephen P.A. Fodor, Glenn Fu, Geoffrey Richard Facer, and Julie Wilhelmy. A true and accurate copy of the '645 patent is attached as **Exhibit 8**.

226. The invention of the '645 patent is directed in general to methods for associating a single cell with a single bead, the single bead comprising a plurality of oligonucleotides (*i.e.*, at least 100 oligonucleotides) comprising an identical cellular label sequence, a target-binding region, and different molecular label sequences.

227. Claim 1 of the '645 patent, reproduced below, is representative:

> 1. A method comprising:
>
> associating a single bead with a single cell,

wherein said single bead comprises a plurality of oligonucleotides,

wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region, and

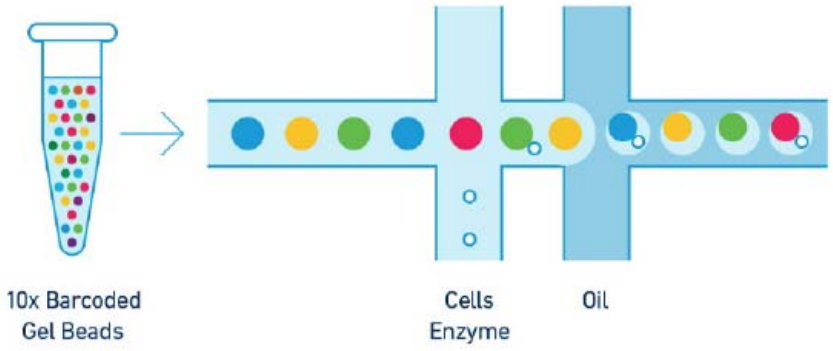
wherein at least 100 of said plurality of oligonucleotides comprise different molecular label sequences.

228. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’645 patent, including at least claim 1 of the ’645 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

229. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ’645 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’645 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

230. The **Single Cell 3’ Workflow** and **Single Cell 5’ Workflow** Accused Products meet the “associating a single bead with a single cell” limitation of claim 1 of the ’645 patent because “[t]he 10x™ GemCode™ Technology partition[s] thousands of cells” with the 10x

Barcoded Gel Beads "into nanoliter-scale Gel Bead-In-EMulsions (GEMs)." [182] As illustrated below, "the cells are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs contains no cell, while the remainder largely contain a single cell."[183]



231. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "wherein said single bead comprises a plurality of oligonucleotides," limitation of claim 1 of the '645 patent because the "Gel Beads are . . . functionalized with millions of copies of a 10x Barcoded primer." [184] The "10x Barcoded primer" is an oligonucleotide ("[e]ach Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1)."[185]). The oligonucleotides of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown in the Figures below[186]:

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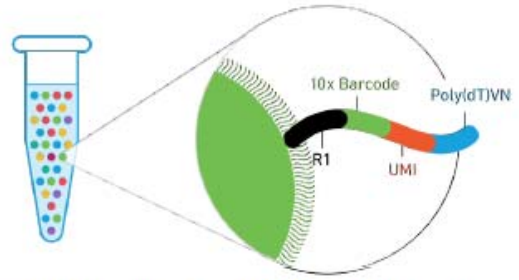
182 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

183 *Id.*

184 *Id.*

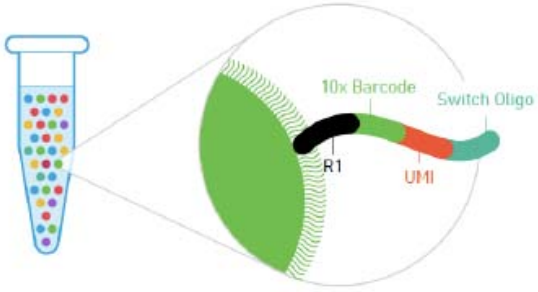
185 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

186 *Id.*



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

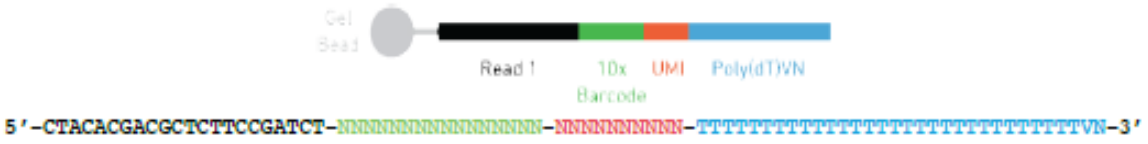
232. The **Single Cell 3' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region," limitation of claim 1 of the '645 patent because each oligonucleotide of each bead comprises a "16nt 10x™ Barcode," (shown in green in Fig. 1 and below[187]) which is a cellular label sequence,[188] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Fig. 1 and below) which is a molecular label sequence, and a "30nt Poly(dT) primer sequence," (shown in blue in Fig. 1 and below) which is a target-binding region.[189] The "16nt 10x™ Barcode," is an identical cellular label sequence because "[t]he 10x™ GemCode™

187 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

188 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

189 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[190] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."

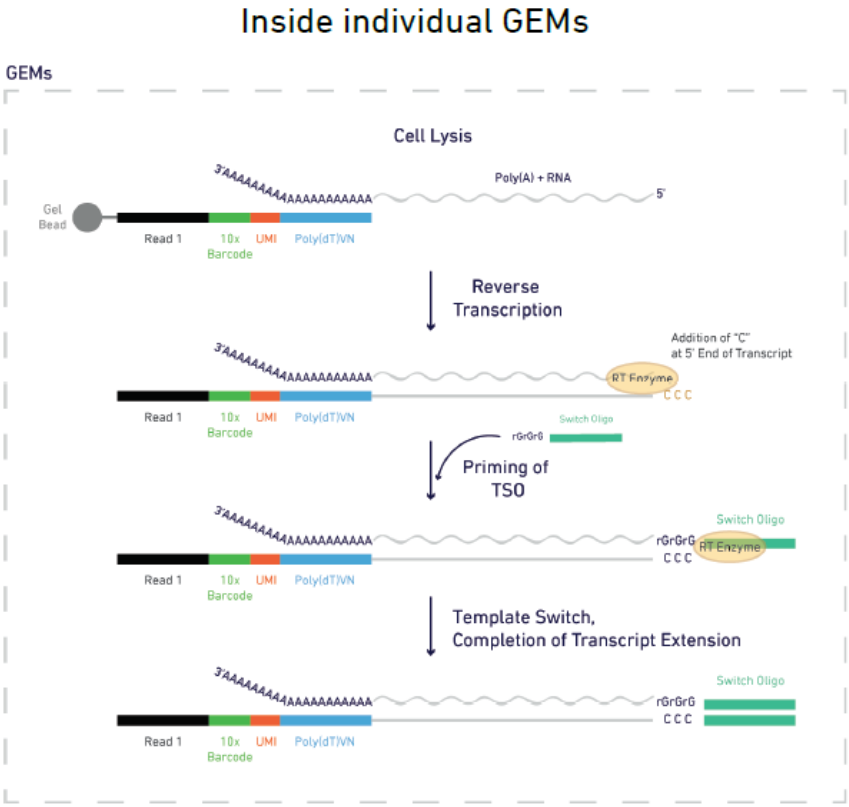


233. As shown below[191], the "30nt Poly(dT) primer sequence" is a target-binding region that binds the poly(A) sequence at the 3' ends of RNA molecules.[192]

[190] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

[191] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped)

[192] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)



234. The **Single Cell 5' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region," limitation of claim 1 of the '645 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in bright green in Figure 1 and below[193]) which is a cellular label sequence,[194] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Figure 1 and below) which is a molecular label sequence, and a "13nt

193 TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Table 1 (cropped)

194 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

Switch Oligo," (shown in dark green in Figure 1 and below) which is a target-binding region.[195] The "16nt 10x™ Barcode," is an identical cellular label sequence because "[t]he 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[196] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."

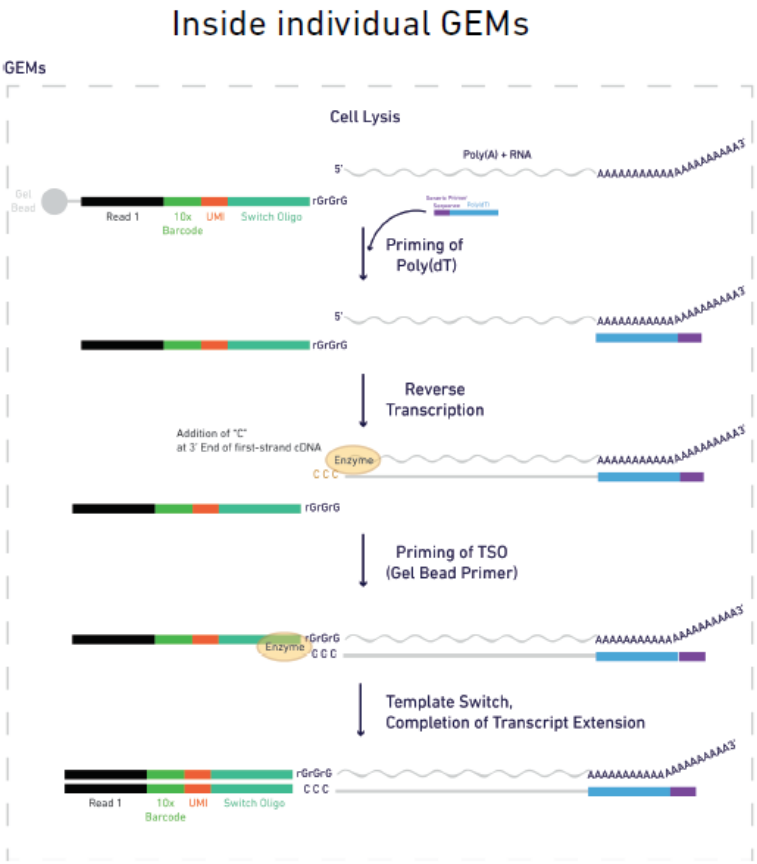
235. As shown below[197], the "13nt Switch Oligo" is a target-binding region that binds the "CCC" sequence at the '3 ends of a cDNA molecule.[198]

[195] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[196] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[197] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped)

[198] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)



236. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "wherein at least 100 of said plurality of oligonucleotides comprise different molecular label sequences" limitation of claim 1 of the '645 patent because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[199] according to a method wherein "[e]ach Gel Bead contains millions of oligo primers."[200]

[199] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052-SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[200] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

237. 10X has also induced and currently induces infringement of at least claim 1 of the '645 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 1 of the '645 patent.[201] 10X has known of the '645 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '645 patent.

238. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '645 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 1 of the '645 patent.[202] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according to at least claim 1 of the '645 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '645 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '645 patent. 10X has knowledge of the '645 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '645 patent.

239. Defendant's infringement has been willful and deliberate because Defendant has known of the '645 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '645 patent.

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[201] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[202] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

240. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 9
(INFRINGEMENT OF THE '646 PATENT)

241. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

242. U.S. Patent No. 9,567,646 (the "'646 patent"), entitled "Massively Parallel Single Cell Analysis," was duly and legally issued on February 14, 2017 to inventors Christina Fan, Stephen P.A. Fodor, Glenn Fu, Geoffrey Richard Facer, and Julie Wilhelmy. A true and accurate copy of the '646 patent is attached as **Exhibit 9**.

243. The invention of the '646 patent is directed in general to a single cell and a single bead, the single bead comprising a plurality of oligonucleotides (*i.e.*, at least 100 oligonucleotides) comprising an identical cellular label sequence, a target-binding region, and different molecular label sequences.

244. Claim 1 of the '646 patent, reproduced below, is representative:

> 1. A composition comprising:
>
> a single cell and a single bead,
>
> wherein said single bead comprises a plurality of oligonucleotides,
>
> wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region, and

wherein at least 100 of said plurality of oligonucleotides comprise different molecular label sequences.

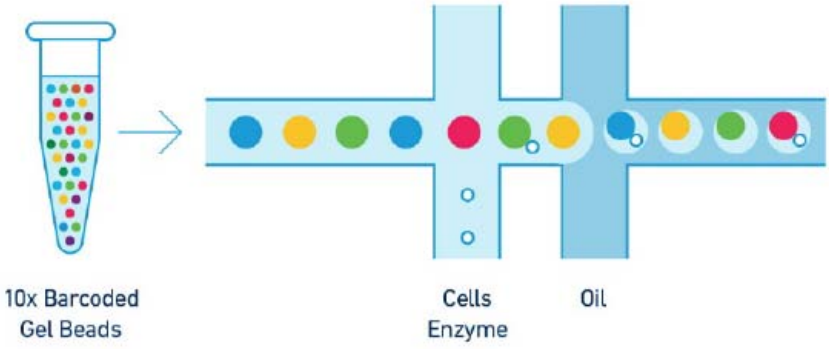
245. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’646 patent, including at least claim 1 of the ’646 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

246. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ’646 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’646 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

247. The **Single Cell 3’ Workflow** and **Single Cell 5’ Workflow** Accused Products meet the “a single cell and a single bead” limitation of claim 1 of the ‘646 patent because “[t]he 10x™ GemCode™ Technology partition[s] thousands of cells” with the 10x Barcoded Gel Beads “into nanoliter-scale Gel Bead-In-EMulsions (GEMs).” [203] As illustrated below, “the cells

[203] “Chromium™ Single Cell 3’ Reagent Kits v2 User Guide” (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); “Chromium™ Single Cell V(D)J Reagent Kits User Guide” (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs contains no cell, while the remainder largely contain a single cell."[204]



248. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "wherein said single bead comprises a plurality of oligonucleotides," limitation of claim 1 of the '646 patent because "Gel Beads are . . . functionalized with millions of copies of a 10x Barcoded primer."[205] The "10x Barcoded primer" is an oligonucleotide ("[e]ach Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1)."[206]). The oligonucleotides of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown in the Figures below[207]:

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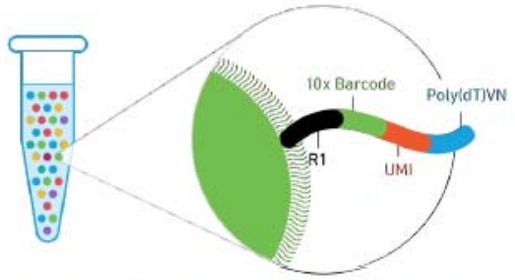
204 *Id.*

205 *Id.*

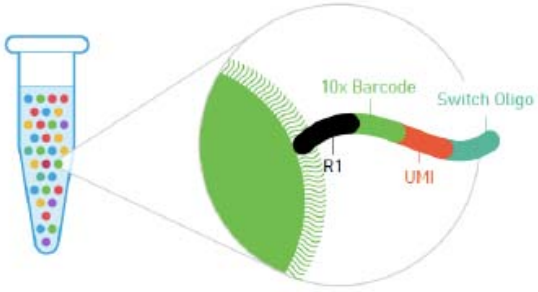
206 " TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

207 *Id.*



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

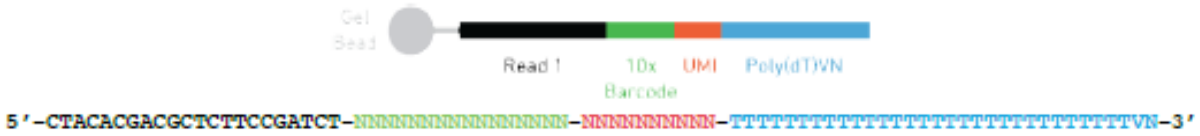
249. The **Single Cell 3' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region," limitation of claim 1 of the '646 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in green in Fig. 1 and below[208]) which is a cellular label sequence,[209] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Fig. 1 and below) which is a molecular label sequence, and a "30nt Poly(dT) primer sequence," (shown in blue in Fig. 1 and below) which is a target-binding region.[210] The "16nt 10x™ Barcode," is an identical cellular label sequence because "[t]he 10x™ GemCode™

[208] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

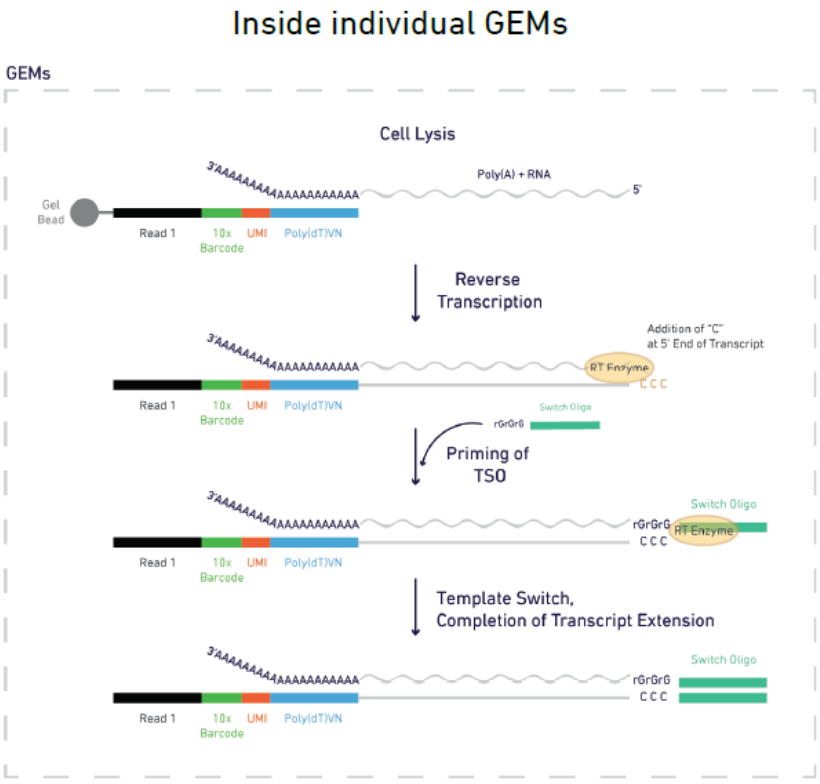
[209] "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

[210] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[211] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."



250. As shown below[212], the "30nt Poly(dT) primer sequence" is a target-binding region that binds the poly(A) sequence at the 3' ends of RNA molecules.[213]



211 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

212 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped)

213 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

251. The **Single Cell 5' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region," limitation of claim 1 of the '646 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in bright green in Figure 1 and below[214]) which is a cellular label sequence,[215] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Figure 1 and below) which is a molecular label sequence, and a "13nt Switch Oligo," (shown in dark green in Figure 1 and below) which is a target-binding region.[216] The "16nt 10x™ Barcode," is an identical cellular label sequence because "[t]he 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[217] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."

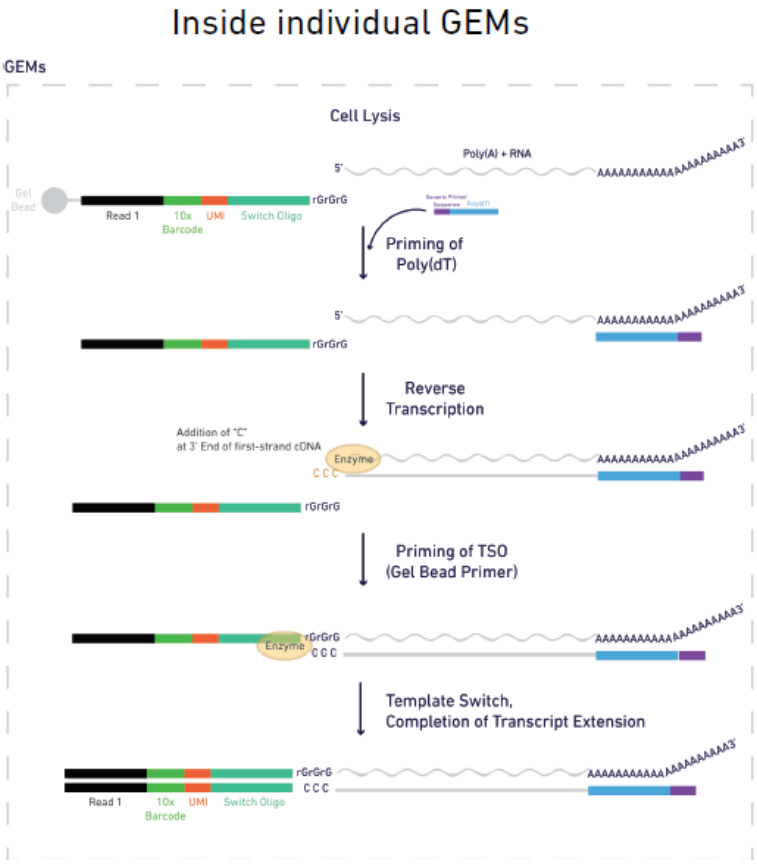
214 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Table 1 (cropped)

215 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

216 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

217 "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

252. As shown below[218], the "13nt Switch Oligo" is a target-binding region that binds the "CCC" sequence at the '3 ends of a cDNA molecule.[219]



253. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "wherein at least 100 of said plurality of oligonucleotides comprise different molecular label sequences" limitation of claim 1 of the '646 patent because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's

218 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped)

219 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pd)

transcriptome"[220] according to a method wherein "[e]ach Gel Bead contains millions of oligo primers."[221]

254. 10X has also induced and currently induces infringement of at least claim 1 of the '646 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, induces customers to use a composition that infringes at least claim 1 of the '646 patent. 10X has known of the '646 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '646 patent.

255. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '646 patent. 10X has designed the Accused Products specifically to be used with the composition as claimed at least claim 1 of the '646 patent. As such, the Accused Products are a material component of the patented combination, specifically designed for use with the composition of at least claim 1 of the '646 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '646 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '646 patent. 10X has knowledge of the '646 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '646 patent.

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[220] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[221] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.docx)

256. Defendant's infringement has been willful and deliberate because Defendant has known of the '137 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '646 patent.

257. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 10
(INFRINGEMENT OF THE '736 PATENT)

258. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

259. U.S. Patent No. 9,598,736 (the "'736 patent"), entitled "Massively Parallel Single Cell Analysis," was duly and legally issued on March 21, 2017 to inventors Christina Fan, Stephen P.A. Fodor, Glenn Fu, Geoffrey Richard Facer, and Julie Wilhelmy. A true and accurate copy of the '736 patent is attached as **Exhibit 10**.

260. The invention of the '736 patent is directed in general to a particle comprising a plurality of oligonucleotides (*i.e.*, at least 100 oligonucleotides) comprising an identical cellular label sequence, a target-binding region, and different molecular label sequences.

261. Claim 16 of the '736 patent, reproduced below, is representative:

> 16. A kit comprising
>
> a plurality of particles
>
> each comprising a plurality of oligonucleotides,

wherein each of the plurality of oligonucleotides comprises a cellular label sequence, a molecular label sequence, and a target-binding region,

wherein the cellular label sequence of each of the plurality of oligonucleotides is the same, and

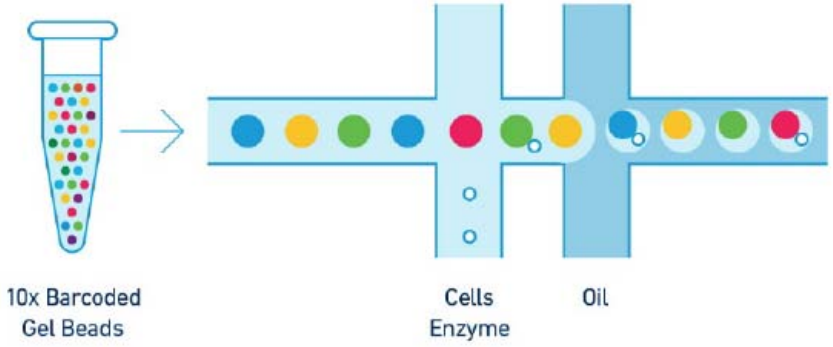
at least 100 of the plurality of oligonucleotides comprise different molecular label sequences.

262. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’736 patent, including at least claim 16 of the ’736 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

263. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 16 of the ’736 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’736 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

264. The **Single Cell 3’ Workflow** and **Single Cell 5’ Workflow** Accused Products meet the “[a] kit comprising a plurality of particles” limitation of claim 16 of the ’736 patent

because the "Chromium™ Single Cell 3' Reagent Kits" include "Single Cell 3' Gel Beads,"[222] and the "Chromium™ Single Cell V(D)J Reagent Kits" include "Single Cell 5' Gel Beads."[223] The "Single Cell 3' Gel Beads," and the "Single Cell 5' Gel Beads" are a plurality of particles as shown below[224].



265. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "each [of the plurality of particles] comprising a plurality of oligonucleotides," limitation of claim 16 of the '736 patent because "Gel Beads are . . . functionalized with millions of copies of a 10x Barcoded primer." [225] The "10x Barcoded primer" is an oligonucleotide ("[e]ach Gel Bead contains millions of oligo primers that are comprised of the following

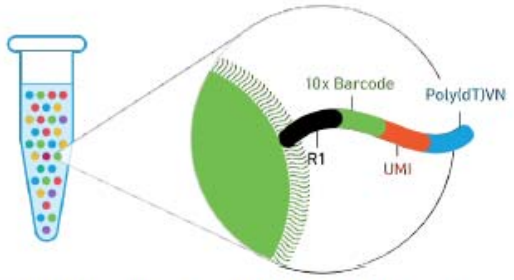
[222] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

[223] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[224] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

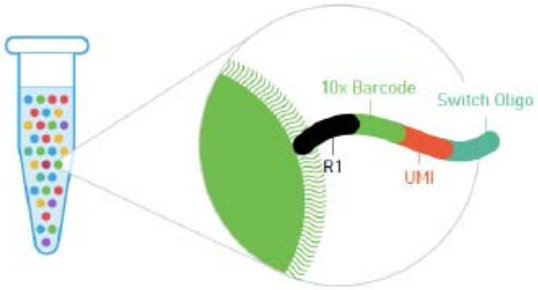
[225] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

sequences (Figure 1)."[226]). The oligonucleotides of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown in the Figures below[227]:



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

266. The **Single Cell 3' Workflow** Accused Products meet the "wherein each of the plurality of oligonucleotides comprises a cellular label sequence, a molecular label sequence, and a target-binding region, wherein the cellular label sequence of each of the plurality of oligonucleotides is the same," limitation of claim 16 of the '736 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in green in Fig. 1 and below[228]) which is a cellular label sequence,[229] a "10nt Unique Molecular Identifier (UMI),"

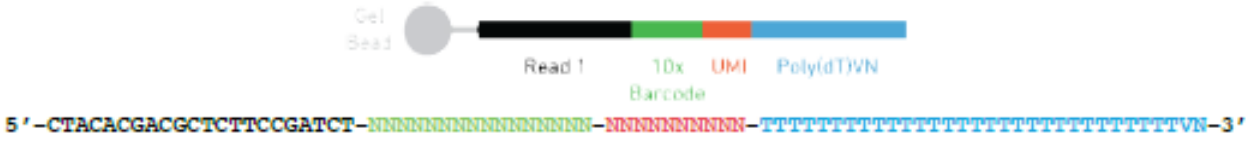
[226] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[227] *Id.*

[228] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

(shown in red in Fig. 1 and below) which is a molecular label sequence, and a "30nt Poly(dT) primer sequence," (shown in blue in Fig. 1 and below) which is a target-binding region.[230]

267. The "16nt 10x™ Barcode," is a cellular label sequence which is the same for each of the plurality of oligonucleotides. "The 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[231] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."



268. As shown below[232], the "30nt Poly(dT) primer sequence" is a target-binding region that binds the poly(A) sequence at the 3' ends of RNA molecules.[233]

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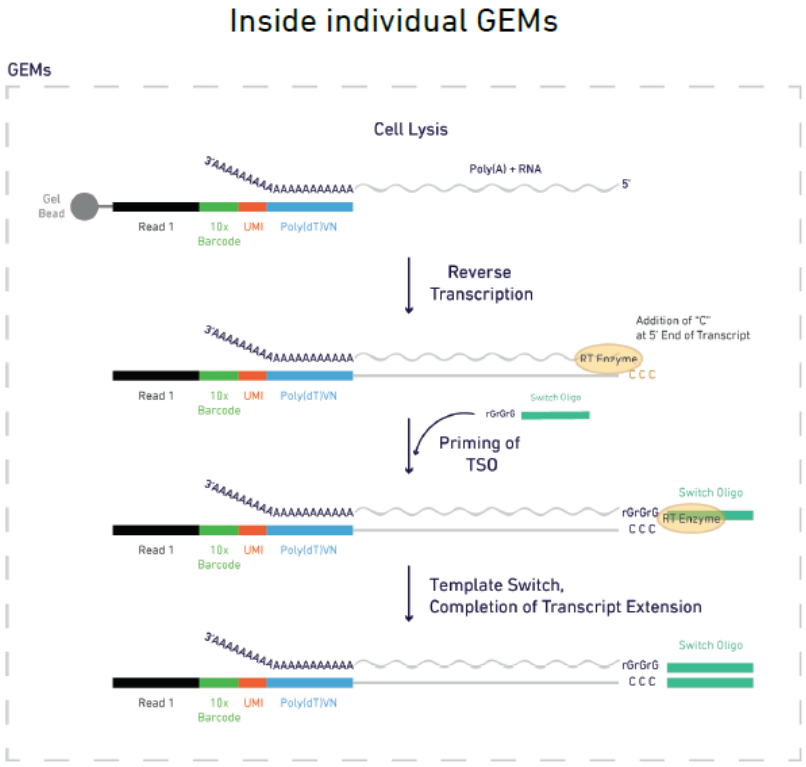
229 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

230 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

231 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

232 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Lib raries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped)

233 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)



269. The **Single Cell 5' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises an identical cellular label sequence, a molecular label sequence, and a target-binding region, wherein the cellular label sequence of each of the plurality of oligonucleotides is the same," limitation of claim 16 of the '736 patent because each oligonucleotide of the bead comprises a "16nt 10x™ barcode," (shown in bright green in Figure 1 and below[234]) which is a cellular label sequence,[235] a "10nt Unique Molecular Identifier

[234] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Table 1 (cropped)

[235] "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

(UMI),” (shown in red in Figure 1 and below) which is a molecular label sequence, and a “13nt Switch Oligo,” (shown in dark green in Figure 1 and below) which is a target-binding region.[236]

270. The “16nt 10x™ Barcode,” is a cellular label sequence which is the same for each of the plurality of oligonucleotides. “The 10x™ GemCode™ Technology . . . separately index[es] each cell’s transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode.”[237] Thus, each oligonucleotide on a particular bead has the same “16nt 10x™ Barcode.”

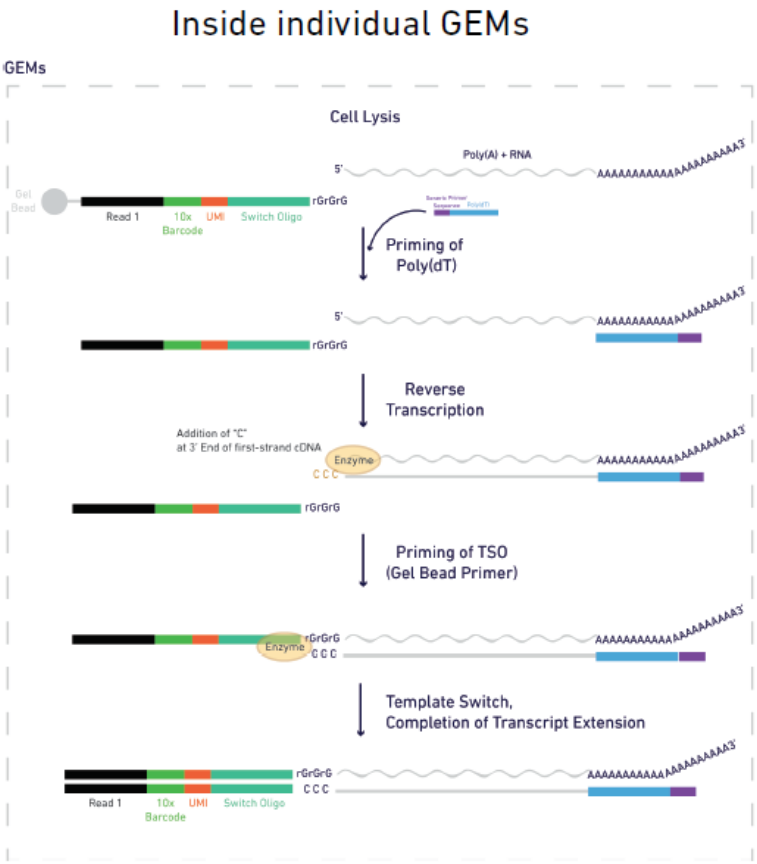
271. As shown below[238], the “13nt Switch Oligo” is a target-binding region that binds the “CCC” sequence at the ’3 ends of a cDNA molecule.[239]

[236] “TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries” (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[237] “Chromium™ Single Cell V(D)J Reagent Kits User Guide” (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[238] “TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries” (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped)

[239] “TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries” (CG000109_AssayConfiguration_VDJ_RevD.pdf)



272. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "at least 100 of the plurality of oligonucleotides comprise different molecular label sequences" limitation of claim 16 of the '736 patent because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[240] according to a method wherein "[e]ach Gel Bead contains millions of oligo primers."[241]

[240] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide": CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf

[241] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

273. 10X has also induced and currently induces infringement of at least claim 16 of the ’736 patent under 35 U.S.C. § 271(b) by providing to customers an instrument the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, induces customers to use a kit that infringes at least claim 16 of the ’736 patent. 10X has known of the ’736 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the ’736 patent.

274. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 16 of the ’736 patent. 10X has designed the Accused Products specifically to be used with the kit as claimed at least claim 16 of the ’736 patent. As such, the Accused Products are a material component of the patented combination, specifically designed for use with the kit of at least claim 16 of the ’736 patent, and especially made and adapted for use in a manner that infringes at least claim 16 of the ’736 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 16 of the ’736 patent. 10X has knowledge of the ’736 patent and is aware that the Accused Products are especially made to be used in a system that infringes the ’736 patent.

275. Defendant’s infringement has been willful and deliberate because Defendant has known of the ’736 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the ’736 patent.

276. As the direct and proximate result of Defendant’s conduct, Plaintiffs have suffered and, if Defendant’s conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because

Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 11
(INFRINGEMENT OF THE '799 PATENT)

277. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

278. U.S. Patent No. 9,637,799 (the "'799 patent"), entitled "Massively Parallel Single Cell Analysis," was duly and legally issued on May 2, 2017 to inventors Christina Fan, Stephen P.A. Fodor, Glenn Fu, Geoffrey Richard Facer, and Julie Wilhelmy. A true and accurate copy of the '799 patent is attached as **Exhibit 11**.

279. The invention of the '799 patent is directed in general to a droplet comprising a single bead and a single cell, the single bead comprising a plurality of oligonucleotides (*i.e.*, at least 100 oligonucleotides) comprising an identical cellular label sequence, an oligo dT sequence, and different molecular label sequences, lysing said single cell to release nucleic acid targets, and attaching the nucleic acid targets to the oligonucleotides.

280. Claim 1 of the '799 patent, reproduced below, is representative:

> 1. A droplet comprising:
>
> a. a single bead comprising
>
> a plurality of oligonucleotides,
>
> wherein each of the plurality of oligonucleotides comprises a molecular label sequence, a cellular label sequence, and an oligo dT sequence, and
>
> wherein the cellular label sequence of each of the plurality of oligonucleotides is the same, and

at least 100 of the plurality of oligonucleotides comprise different molecular label sequences; and

b. a single cell.

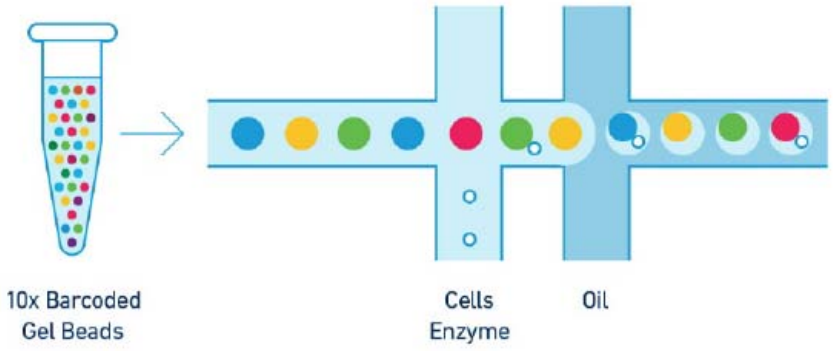
281. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’799 patent, including at least claim 1 of the ’799 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

282. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 1 of the ’799 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’799 patent claims, including by making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

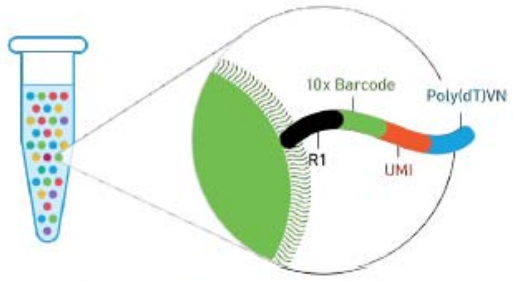
283. The **Single Cell 3’ Workflow** Accused Products meet the “droplet comprising: a. a single bead” limitation (a) “a single cell” limitation (b) of claim 1 of the ’799 patent because “[t]he 10x™ GemCode™ Technology partition[s] thousands of cells” with the 10x Barcoded Gel Beads “into nanoliter-scale Gel Bead-In-EMulsions (GEMs).” [242] As illustrated below, “the cells are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs

[242] “Chromium™ Single Cell 3’ Reagent Kits v2 User Guide” (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

contains no cell, while the remainder largely contain a single cell."[243] The "nanoliter-scale Gel Bead-In-EMulsions (GEMs) " is a droplet because it is a "single nanoliter reaction volume[] partitioned by oil."[244]



284. The **Single Cell 3' Workflow** Accused Products meet the "a single bead comprising a plurality of oligonucleotides," limitation (a) of claim 1 of the '799 patent because the "Gel Beads are . . . functionalized with millions of copies of a 10x Barcoded primer."[245] The "10x Barcoded primer" is an oligonucleotide ("[e]ach Gel Bead contains millions of oligo primers that are comprises of the following sequences (Figure 1)."[246]). The oligonucleotides of the Gel Beads for the **Single Cell 3' Workflow** Accused Products are shown in Fig. 1 below[247]:



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.

243 *Id.*

244 *Id.*

245 *Id.*

246 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

247 *Id.*

285. The **Single Cell 3' Workflow** Accused Products meet the "wherein each of the plurality of oligonucleotides comprises a molecular label sequence, a cellular label sequence, and an oligo dT sequence, and wherein the cellular label sequence of each of the plurality of oligonucleotides is the same" limitation (a) of claim 1 of the '799 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in green in Fig. 1 and below[248]) which is a cellular label sequence,[249] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Fig. 1 and below) which is a molecular label sequence, and a "30nt Poly(dT) primer sequence," (shown in blue in Fig. 1 and below) which is an oligo dT sequence.[250]

286. The "16nt 10x™ Barcode," is a cellular label sequence which is the same for each of the plurality of oligonucleotides. "The 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[251] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."

248 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

249 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

250 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

251 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

287. The **Single Cell 3' Workflow** Accused Products meet the "at least 100 of the plurality of oligonucleotides comprise different molecular label sequences" limitation (a) of claim 1 of the '799 patent because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's transcriptome"[252] according to a method wherein "[e]ach Gel Bead contains millions of oligo primers."[253]

288. 10X has also induced and currently induces infringement of at least claim 1 of the '799 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along with directions for use that, when followed in an intended manner and in a normal mode of operation, induces customers to use a composition that infringes at least claim 1 of the '799 patent.[254] 10X has known of the '799 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '799 patent.

289. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 1 of the '799 patent. 10X has designed the Accused Products specifically to be used with the composition as claimed at least claim 1 of the '799 patent. As such, the Accused Products are a material component of the patented combination, specifically designed for use with the composition of at least claim 1 of the '799 patent, and especially made and adapted for use in a manner that infringes at least claim 1 of the '799 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 1 of the '799 patent. 10X has knowledge of the '799 patent and is aware

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252 *Id.*

253 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

254 *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

that the Accused Products are especially made to be used in a system that infringes the '799 patent.

290. Defendant's infringement has been willful and deliberate because Defendant has known of the '799 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '799 patent.

291. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

COUNT 12
(INFRINGEMENT OF THE '799 PATENT)

292. Plaintiffs incorporate all of the above paragraphs as though fully set forth herein.

293. The '799 patent, entitled "Massively Parallel Single Cell Analysis," was duly and legally issued on May 2, 2017 to inventors Christina Fan, Stephen P.A. Fodor, Glenn Fu, Geoffrey Richard Facer, and Julie Wilhelmy. A true and accurate copy of the '799 patent is attached as **Exhibit 11**.

294. The invention of the '799 patent is directed in general to methods for introducing a single cell and a single bead into a droplet, the single bead comprising a plurality of oligonucleotides (*i.e.,* at least 100 oligonucleotides) comprising an identical cellular label sequence, a target-binding region, and different molecular label sequences, lysing said single cell to release nucleic acid targets, and attaching the nucleic acid targets to the oligonucleotides.

295. Claim 17 of the ’799 patent, reproduced below, is representative:

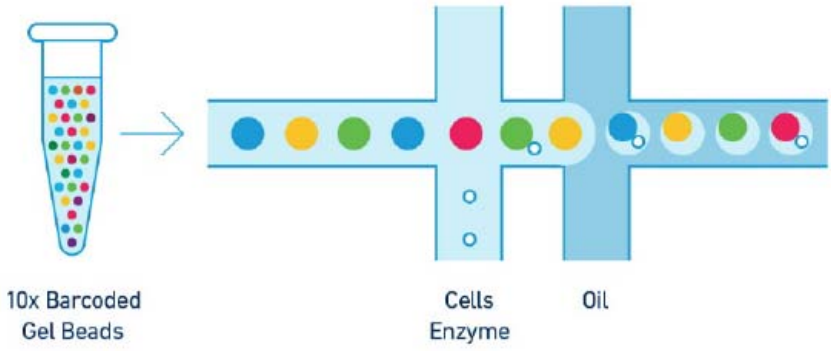
> 17. A method comprising:
>
> a. introducing a single cell and a single bead into a droplet,
>
> wherein said single bead comprises a plurality of oligonucleotides,
>
> wherein each of the plurality of oligonucleotide comprises a cellular label sequence, a target-binding region, and a molecular label sequence, and
>
> wherein the cellular label sequence of each of the plurality of oligonucleotides is the same and
>
> at least 100 of the plurality of oligonucleotides comprises different molecular label sequences;
>
> b. lysing said single cell, thereby releasing nucleic acid targets from said cell; and
>
> c. attaching said nucleic acid targets to said plurality of oligonucleotides.

296. On information and belief, as set forth below, Defendant, directly or through the actions of its employees, divisions, and/or subsidiaries, has infringed and continues to infringe one or more claims of the ’799 patent, including at least claim 17 of the ’799 patent directly, indirectly, literally, and/or by equivalents under 35 U.S.C. *et seq*, including, but not limited to § 271 by, among other things, importing the Accused Products and/or making, using, offering for sale, and selling the Accused Products in the United States or inducing or contributing to such acts.

297. As demonstrated below, the Accused Products satisfy the claim limitations of at least claim 17 of the ’799 patent. The demonstration of infringement illustrated below is offered by way of example only and without limitation to BD’s ability to demonstrate Defendant’s direct, indirect, literal, or equivalent infringement of additional ’799 patent claims, including by

making, using, selling, offering for sale, or importing additional products or inducing or contributing to such acts.

298. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "introducing a single cell and a single bead into a droplet" limitation (a) of claim 17 of the '799 patent because "[t]he 10x™ GemCode™ Technology partition[s] thousands of cells" with the 10x Barcoded Gel Beads "into nanoliter-scale Gel Bead-In-EMulsions (GEMs)."[255] As illustrated below, "the cells are delivered at a limiting dilution, such that the majority (~90-99%) of generated GEMs contains no cell, while the remainder largely contain a single cell."[256] The "nanoliter-scale Gel Bead-In-EMulsions (GEMs) "is a droplet because it is a "single nanoliter reaction volume[] partitioned by oil."[257]



299. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "wherein said single bead comprises a plurality of oligonucleotides," limitation (a) of claim 17 of the '799 patent because the "Gel Beads are . . . functionalized with millions of copies

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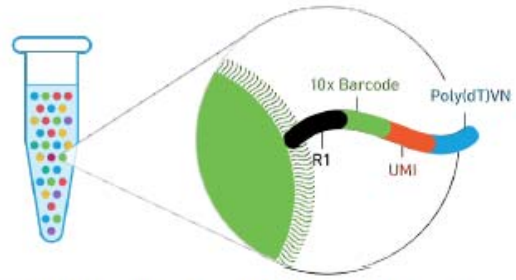
255 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

256 *Id.*

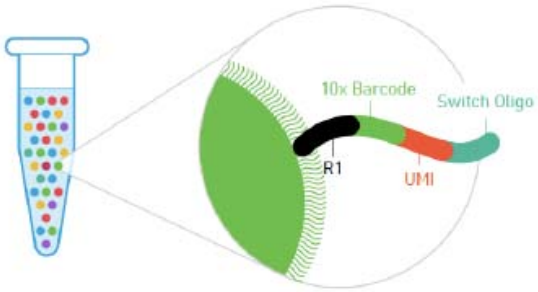
257 *Id.*

of a 10x Barcoded primer." [258] The "10x Barcoded primer" is an oligonucleotide ("[e]ach Gel Bead contains millions of oligo primers that are comprised of the following sequences (Figure 1)."[259]). The oligonucleotides of the Gel Beads for the **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products are shown in the Figures below[260]:



i. Partial Illumina Read 1 sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 30 nt Poly(dT) primer sequence

Fig. 1. Schematic of a SC3' v2 Gel Bead oligo primer.



i. Partial Illumina Read 1 Sequence (22 nucleotides (nt))
ii. 16 nt 10x™ Barcode
iii. 10 nt Unique Molecular Identifier (UMI)
iv. 13 nt Switch Oligo

Figure 1. Schematic of a Single Cell 5' Gel Bead oligo primer.

300. The **Single Cell 3' Workflow** Accused Products meet the "wherein each of the plurality of oligonucleotides comprises a cellular label sequence, a target-binding region, and a molecular label sequence , and wherein the cellular label sequence of each of the plurality of oligonucleotides is the same" limitation (a) of claim 17 of the '799 patent because each oligonucleotide of the bead comprises a "16nt 10x™ Barcode," (shown in green in Fig. 1 and

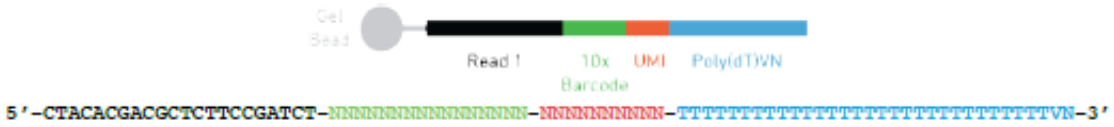
258 *Id.*

259 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

260 *Id.*

below[261]) which is a cellular label sequence,[262] a "10nt Unique Molecular Identifier (UMI)," (shown in red in Fig. 1 and below) which is a molecular label sequence, and a "30nt Poly(dT) primer sequence," (shown in blue in Fig. 1 and below) which is a target-binding region.[263]

301. The "16nt 10x™ Barcode," is a cellular label sequence which is the same for each of the plurality of oligonucleotides. "The 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[264] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."



302. As shown below[265], the "30nt Poly(dT) primer sequence" is a target-binding region that binds the poly(A) sequence at the 3' ends of RNA molecules.[266]

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261 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 4 (cropped)

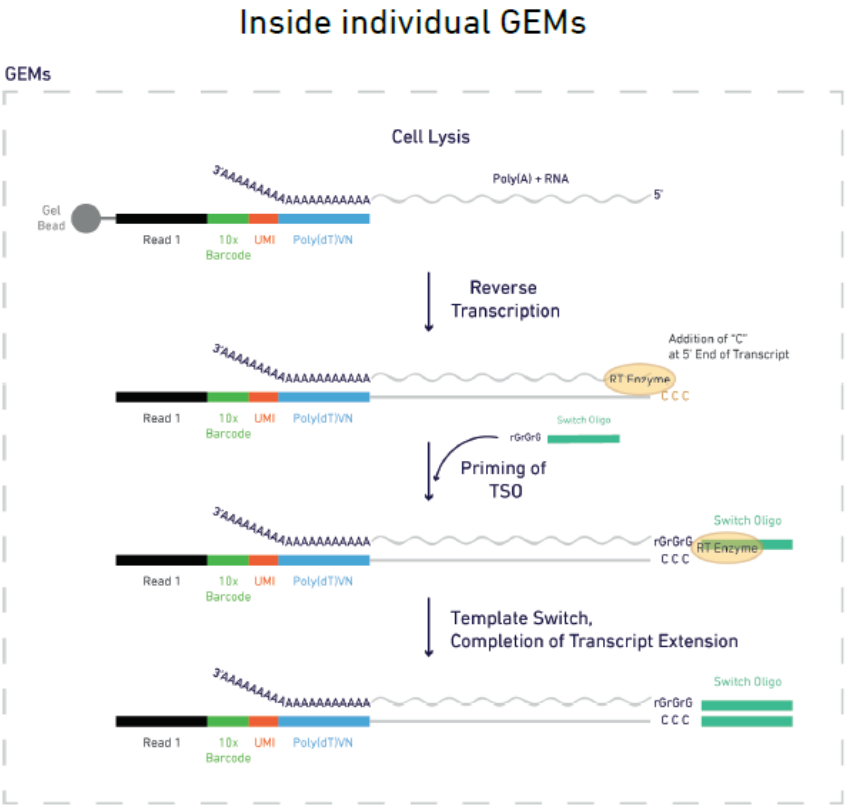
262 "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell 3' Reagent Kits v2 User Guide": CG00052 SingleCell3'ReagentKitv2UserGuide_RevD.pdf

263 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)

264 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

265 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped)

266 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf)



303. The **Single Cell 5' Workflow** Accused Products meet the "wherein each of said plurality of oligonucleotides comprises a cellular label sequence, a target-binding region, and a molecular label sequence, and wherein the cellular label sequence of each of the plurality of oligonucleotides is the same," limitation (a) of claim 17 of the '799 patent because each oligonucleotide of the bead comprises a "16nt 10x barcode," (shown in bright green in Figure 1 and below[267]) which is a cellular label sequence,[268] a "10nt Unique Molecular Identifier (UMI),"

[267] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Table 1 (cropped)

[268] "[A]ll generated cDNA share a common 10x Barcode. Libraries are generated and sequenced from the cDNA and the 10x Barcodes are used to associate individual reads back to the individual partitions." *See* "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

(shown in red in Figure 1 and below) which is a molecular label sequence, and a "13nt Switch Oligo," (shown in dark green in Figure 1 and below) which is a target-binding region.[269]

304. The "16nt 10x™ Barcode," is a cellular label sequence which is the same for each of the plurality of oligonucleotides. "The 10x™ GemCode™ Technology . . . separately index[es] each cell's transcriptome. It does so by partitioning thousands of cells into nanoliter-scale Gel Bead-In-EMulsions (GEMs), where all generated cDNA share a common 10x Barcode."[270] Thus, each oligonucleotide on a particular bead has the same "16nt 10x™ Barcode."

305. As shown below[271], the "13nt Switch Oligo" is a target-binding region that binds the "CCC" sequence at the '3 ends of a cDNA molecule.[272]

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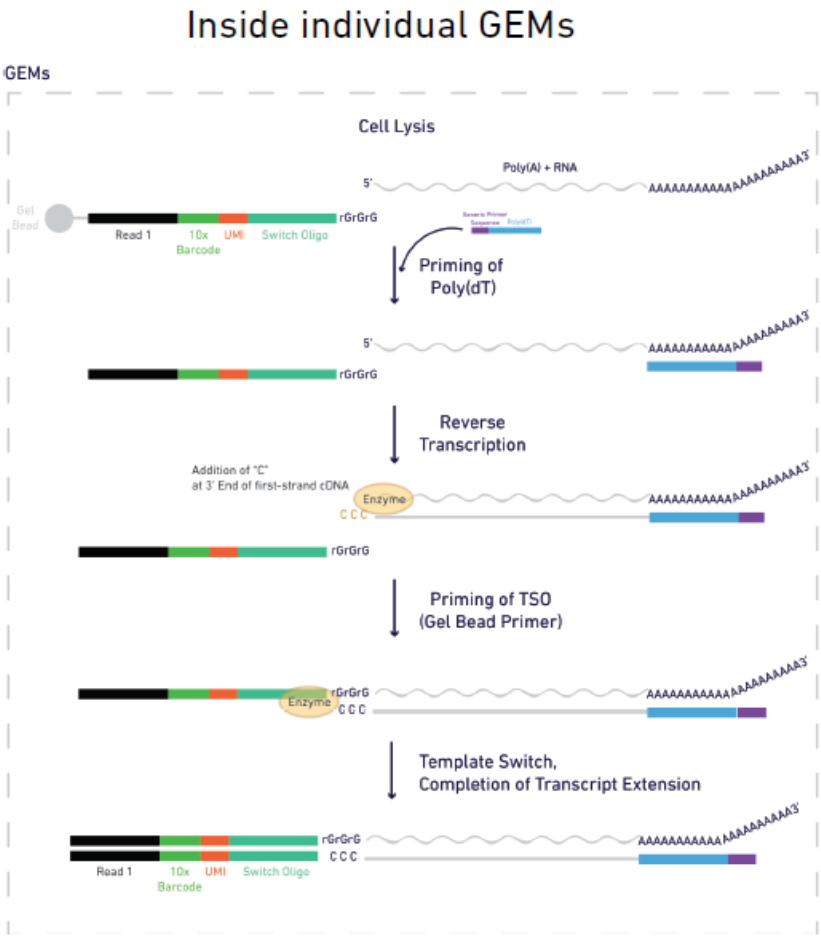
269 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

270 "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

271 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped)

272 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)



306. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "at least 100 of said plurality of oligonucleotides comprise different molecular label sequences" limitation (a) of claim 17 of the '799 patent because "[t]he 10x™ GemCode™ Technology samples a pool of ~ 750000 barcodes to separately index each cell's

transcriptome"[273] according to a method wherein "[e]ach Gel Bead contains millions of oligo primers."[274]

307. The **Single Cell 3' Workflow** and **Single Cell 5' Workflow** Accused Products meet the "lysing said single cell, thereby releasing nucleic acid targets from said cell" limitation (b) of claim 17 of the '799 patent because "[o]nce partitioned, the Gel Bead dissolves and its oligo primers are released into the aqueous environment of the GEM. The cell captured in the GEM is also lysed. The contents of the GEM (oligos, lysed cell components and Master Mix) are incubated in an RT reaction to generate full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[275] The poly A-tailed mRNA transcripts are nucleic acid targets release from the cell.

308. The **Single Cell 3' Workflow** Accused Products meet the "attaching said nucleic acid targets to said plurality of oligonucleotides" limitation (c) of claim 17 of the '799 patent because "[u]pon dissolution of the Single Cell 3' Gel Bead in a GEM, primers . . . are released and mixed with cell lysate and Master Mix. Incubation of the GEMs then produces barcoded, full-length cDNA from poly-adenylated mRNA."[276] As shown below,[277] the poly A-tailed

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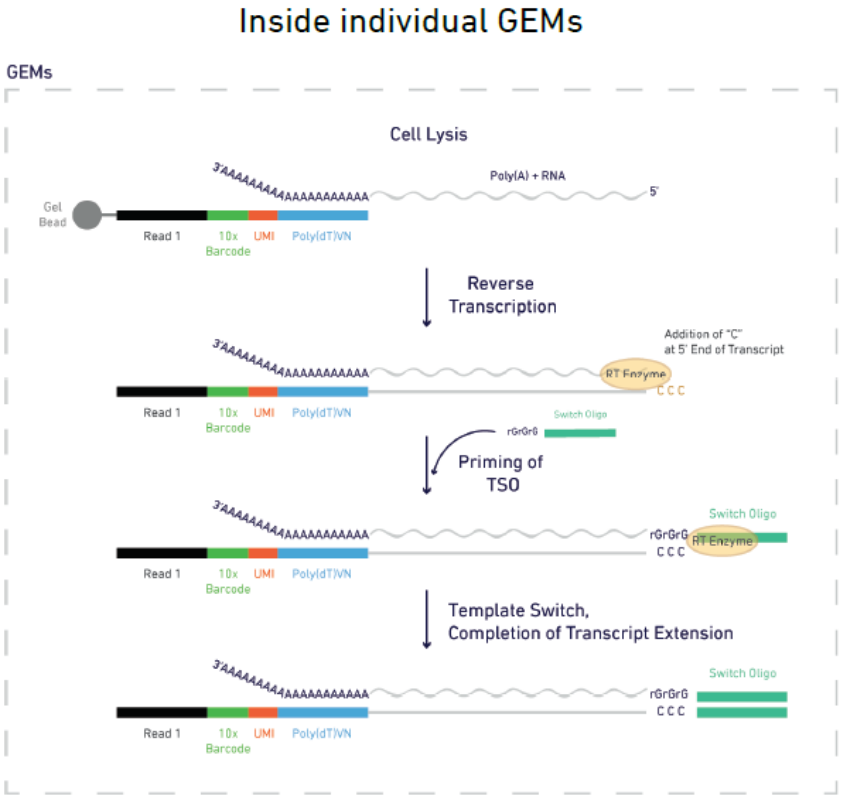
[273] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[274] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[275] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf); "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf)

[276] "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG 00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

mRNA transcripts released from lysing the cell hybridize to the "30nt Poly(dT) primer sequence" and are thus attached to said plurality of oligonucleotides. The subsequent reverse transcriptase reaction "generate[s] full-length, barcoded cDNA from the poly A-tailed mRNA transcripts."[278]

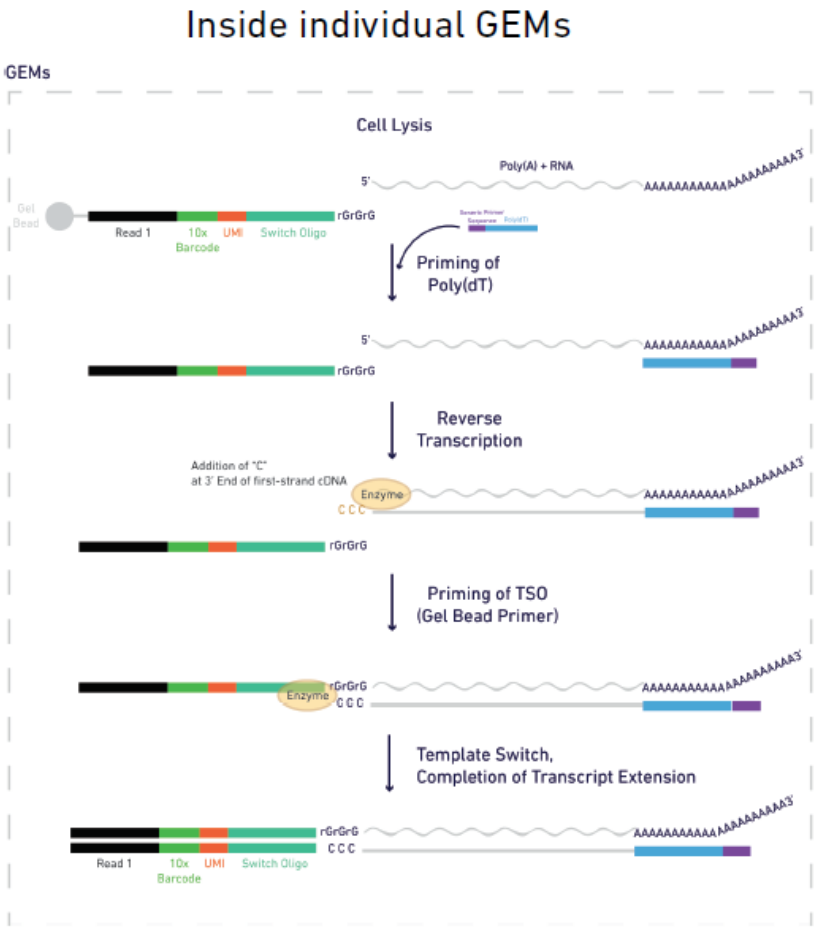


309. The **Single Cell 5' Workflow** Accused Products meet the "attaching said nucleic acid targets to said plurality of oligonucleotides" limitation (c) of claim 17 of the '799 patent because "[u]pon dissolution of the Single Cell 5' Gel Bead in a GEM, oligonucleotides . . . are released and mixed with cell lysate and Master Mix that contains reverse transcription (RT) reagents and poly(dT) primers. Incubation of the GEMs then produces barcoded, full-length

277 "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell 3' v2 Libraries" (CG000108_AssayConfiguration_SC3v2.pdf) at Figure 3 (cropped)

278 "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3_ReagentKitv2UserGuide_RevD.pdf)

cDNA from poly-adenylated mRNA."[279] As shown below,[280] the poly A-tailed mRNA transcripts released from lysing the cell are reverse transcribed into cDNA, the 3' end of which hybridizes to the "13nt Switch Oligo." Thus, the poly A-tailed mRNA transcripts released from lysing the cell are attached to said plurality of oligonucleotides via hybridization with the cDNA which is hybridized to the "13nt Switch Oligo" of the plurality of oligonucleotides.



310. 10X has also induced and currently induces infringement of at least claim 17 of the '799 patent under 35 U.S.C. § 271(b) by providing to customers the Accused Products, along

[279] "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[280] "TECHNICAL NOTE Assay Scheme and Configuration of Chromium™ Single Cell V(D)J Libraries" (CG000109_AssayConfiguration_VDJ_RevD.pdf) at Figure 3 (cropped)

with directions for use that, when followed in an intended manner and in a normal mode of operation, 10X knows infringes at least claim 17 of the '799 patent.[281] 10X has known of the '799 patent and of its infringement of that patent since at least May 2017. By providing its customers with the Accused Products and those directions for use, 10X specifically intends that its customers infringe the '799 patent.

311. 10X has contributorily infringed and currently contributorily infringes under 35 U.S.C. § 271(c) at least claim 17 of the '799 patent. 10X has designed the Accused Products specifically to be used in a manner as claimed at least claim 17 of the '799 patent.[282] As such, the Accused Products are a material component of the patented combination, specifically designed to be used according to at least claim 17 of the '799 patent, and especially made and adapted for use in a manner that infringes at least claim 17 of the '799 patent. The Accused Products are not staple articles of commerce and they do not have substantial uses that do not infringe at least claim 17 of the '799 patent. 10X has knowledge of the '799 patent and is aware that the Accused Products are especially made to be used in a system that infringes the '799 patent.

312. Defendant's infringement has been willful and deliberate because Defendant has known of the '799 patent since at least May 2017 and knew or should have known of its infringement but acted despite an objectively high likelihood that such acts would infringe the '799 patent.

313. As the direct and proximate result of Defendant's conduct, Plaintiffs have suffered and, if Defendant's conduct is not stopped, will continue to suffer, severe competitive

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[281] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

[282] *See, e.g.*, "Chromium™ Single Cell 3' Reagent Kits v2 User Guide" (CG00052_SingleCell3'ReagentKitv2UserGuide_RevD.pdf); "Chromium™ Single Cell V(D)J Reagent Kits User Guide" (CG000086_SingleCellVDJReagentKitsUserGuide_RevD.pdf)

harm, irreparable injury, and significant damages, in an amount to be proven at trial. Because Plaintiffs' remedy at law is inadequate, Plaintiffs seek, in addition to damages and injunctive relief. Plaintiffs' business operates in a competitive market and will continue suffering irreparable harm absent injunctive relief.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs BD and Cellular Research pray for relief and judgment that:

a. 10X has infringed the Asserted Patents;

b. Plaintiffs are entitled to preliminary and permanent injunctive relief enjoining 10X, its officers, agents, servants, and employees, and those persons in active concert or participation with any of them, from manufacturing, using, offering for sale, selling in the United States, or importing into the United States, the Accused Products, and any other product that infringes or induces or contributes to the infringement of the Asserted Patents, prior to the expiration date of the last to expire of those patents;

c. Plaintiffs are entitled to an award of damages pursuant to 35 U.S.C. § 284, including pre-judgment and post-judgment interest;

d. 10X's infringement of the Asserted Patents has been willful and Plaintiffs are entitled to enhanced damages up to and including trebling of the damages awarded to them;

e. Plaintiffs are entitled to their costs and reasonable expenses to the fullest extent permitted by law;

f. This case is exceptional pursuant to 35 U.S.C. § 285, and plaintiffs are entitled to an award of attorneys' fees; and

g. Plaintiffs are entitled to other and further relief as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(b), BD and Cellular Research hereby demand a trial by jury on all issues so triable.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

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