

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.,
Petitioner

v.

10X GENOMICS, INC.,
Patent Owner

Case IPR2023-00955
Patent 10,240,197

**PATENT OWNER'S SUBMISSION OF UNRESOLVED
OBJECTIONS TO PETITIONER'S DEMONSTRATIVES**

Pursuant to 37 C.F.R. §42.70(b), and the Board’s September 24, 2024 Order Setting Oral Argument (Paper 35), Patent Owner 10x Genomics, Inc. (“PO”) respectfully submits the below list of unresolved objections to Petitioner’s demonstratives.¹ Following each objection is a copy of the objected-to slide with objectionable portions within blue rectangles.

¹ PO did not include untimeliness objections to slides containing evidence and argument that were belatedly raised in Petitioner’s Reply or Motion to Exclude, and which reflect issues already addressed by PO in its Sur-Reply and Response in Support of its Motion to Exclude.

- **Slide 37:** The heading of this slide mischaracterizes Patent Owner's arguments relating to Linnarsson's disclosures.

PO's Position Linnarsson Is Limited To Fragmentation And Capture

PO's Sur-Reply

(a) **Linnarsson's STRT Method Consistently Discloses Fragmentation and Capture**

Petitioner again asserts, on Reply, that Linnarsson discloses sequencing the entire tagged polynucleotide, but makes the new argument (contradicting its Petition mapping) that "Linnarsson cannot possibly require fragmentation as in Figure 11," and Figs.3-4 "include neither a biotin nor a restriction enzyme cut site." Rep.6-7. But Linnarsson's fragmentation-and-capture STRT method employs *both* (EX1003, 23:1-37:32; EX2013, ¶¶36-37, 47)—including in Linnarsson's only two examples.⁴ *Ex.I*, which introduces Figs.2-4 (EX1003, 23:9-25:6; EX2040, 25:21-31:9 (agreeing "both Examples 1 and 2 of Linnarsson disclose fragmentation and capture")), and *Ex.II*, which introduces Fig.11 (EX1003, 37:31-32).

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

PO's Sur-Reply at 5
Parse 37

- **Slides 40, 41, 77, 78, 90, 91, 92, 93, 103, 109, 113, 137, 141, 142, 143, 162, 170, 184, 198:** These slides rely on new evidence and arguments relating to the Final Written Decision in IPR2023-00876 that were not previously briefed. [Representative slide below; others are similar in form.]

IPR2023-0876 Decision: Biotin Not Required And The Steps Of Figure 11 Are “Optionally Used”

Final Written Decision

Patent Owner argues that Petitioner’s argument that Linnarsson does not require biotin is a new and improper argument on reply. PO Sur-Reply 19. We disagree. Petitioner’s argument is directly responsive to Patent Owner’s argument. See 37 C.F.R. § 42.23(b) (“A reply may only respond to arguments raised in the corresponding opposition, patent owner preliminary response, patent owner response, or decision on institution.”). Petitioner’s argument is not only proper, but also persuasive; Linnarsson does not require biotin. See Ex. 1003, 3:25–4:2 (“Summary of the Invention” not mentioning biotin), 5:28–29 (“Figure 11 [which does include biotin], panels A–F, show graphical representation of steps optionally used in the STRT method.” (emphasis added)), Figs. 3–4 (not including biotin).

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

IPR2023-00876 Final Written Decision at 53-54

Parse 40

- **Slide 59:** This slide relies on new evidence that is not cited by any paper.

Linnarsson Uses BtsCI

The fragments were released by BtsCI digestion, and simultaneously ligated to the FDV and RDV adapters. The beads were then resuspended in the reaction mix shown in Table 6.

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

EX1003 (WO2010/117620) at 27:7-8

Parse 59

- **Slide 60:** This slide relies on new evidence that is not cited by any paper.

Linnarsson Uses BtsCI

5' fragments containing barcodes and cDNA inserts were released from the beads by **BtsCI** digestion, and adapters were simultaneously ligated to generate a sample suitable for sequencing on the Illumina Genome Analyzer. The beads were resuspended in 40 μ L of 1 mM ATP, 1 μ M SOLEXA-ADP1 adapter

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

EX1003 (WO2010/117620) at 35:28-31
Parse 60

- **Slide 61:** This slide relies on new evidence and argument regarding Linnarsson's disclosures, which is unsupported by citations to merits briefing and is included only in briefing relating to Petitioner's Motion to Exclude, and which fails to include the context of Dr. Cooper's testimony by

omitting the entirety of the question and answer.

Dr. Cooper: Bacteria Use Poly A Tails



“But it is certainly possible one could imagine using a different enzyme, depending on the experimental context. But the only one called out by Linnarsson is BtsC1.”

Gregory Cooper
Parse's Expert

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE
(Patent Owner's Opp to Petitioner's Motion to Exclude)

EX2040 (Cooper Depo) at 35:17-20
Parse 61

- **Slide 62:** This slide relies on new evidence and argument regarding Linnarsson's disclosures, which is unsupported by citations to merits briefing and is included only in briefing relating to Petitioner's Motion to

Exclude.

Dr. Cooper: Bacteria Use Poly A Tails



Gregory Cooper
Parse's Expert

Q. What is your understanding of whether Linnarsson is contemplating use the Bts-I restriction enzyme with any of its approaches?

A. It is -- Bts-I isn't mentioned. That's a different enzyme than the one that is part of the example in Linnarsson.

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE
(Petitioner's Motion to Exclude)

EX2040 (Cooper Depo) at 70:16-22 (objection omitted)
Parse 62

- **Slide 63:** This slide relies on new evidence and argument regarding Linnarsson's disclosures, which is unsupported by citations to merits briefing and is included only in briefing relating to Petitioner's Motion to Exclude.

Dr. Cooper: Bacteria Use Poly A Tails



Gregory Cooper
Parse's Expert

Q. Okay. What's your understanding of whether Linnarsson ever refers to those sequences of nucleotides that happen to correspond to the Bts-I restriction enzyme cut site as a -- as a cut site for use with any of the approaches that are disclosed therein?

A. Again, it doesn't refer to that enzyme. So any -- any use of it would be totally happenstance or coincidental that that sequence happened to appear in the examples of Figures 3 and 4.

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE
(Petitioner's Motion to Exclude)

EX2040 (Cooper Depo) at 71:10-21 (objection omitted)
Parse 63

- **Slide 73:** The heading of this slide mischaracterizes the underlying document and makes a new argument regarding Petitioner's theory, which is not made in any paper.

The Petition: Stated Only That "Entire" Tagged Polynucleotide Was Subjected To Sequencing

The Petition

g. [1G] (c) sequencing the tagged polynucleotide to determine the sample sequence, the first tag sequence, and the second tag sequence; and

Linnarsson teaches that after generating the tagged polynucleotides, "sequencing is performed" thereon. See EX1003 at 4:8-13, 19:28-32, 21:13-25; EX1015 at 8:22-28, 8:33-9:10, 9:35-10:6. A POSA would have understood that such sequencing is performed on the entire tagged polynucleotide, which includes the sample sequence and both tag sequences. EX1002 ¶ 176.

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

'197 Petition at 44
Parse 73

- **Slide 123:** This slide relies on new evidence that is not cited by any paper, and fails to include the context of Dr. Cooper's testimony by omitting the entirety of the question and answer.

Dr. Cooper: Bacteria Use Poly A Tails



Gregory Cooper
Parse's Expert

A. So, no. It's -- again, this is one of those statements that asserts a degree of evidence and proof that really isn't there. And it certainly is true the bacteria used poly-A differently, but it's not fair to say that there's -- for example, they're saying there is no poly-A-tail in bacteria. That's not true.

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

EX2040 (Cooper Depo) at 22:20-23:4
Parse 123

- **Slide 151:** This slide fails to include the context of Dr. Quackenbush's testimony by omitting the entirety of the question and answer.

Dr. Quackenbush: Ligation Was Known And Conventional



John
Quackenbush
10X's Expert

"So ligation is used. Ligation is a method that was known in the art just like PCR was known in the art. But it's a way of carrying out claim 1."

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE
(*197 Reply to POR at 19)

EX1071 (Quackenbush Depo) at 186:6-9
Parse 151

- **Slide 177:** This slide appears to rely on new evidence that is not cited by any paper and new argument to support Petitioner's claim 26 arguments that is not made in any paper.

McCloskey: Teaches Allele Copies

Our method utilizes an encoding oligonucleotide with five distinct informational regions (Fig. 1): (1) the batch-stamp, unique to each experiment, specifies the DNA source such as the patient or sample identification, and the date of reaction; (2) the random barcode distinguishes among sequences arising from different cell or allele copies; (3) the primer-binding site facilitates specific PCR amplification; (4) the genomic target-binding site targets the locus to be encoded prior to amplification; and (5) the extra 5' bases serve as an internal sentinel of recoding. This encoding

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE
(*197 Petition at 9)

EX1004 (McCloskey et al.) at 2
Parse 177

Respectfully submitted,

Dated: November 5, 2024

By: /Megan Raymond/

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of PATENT OWNER'S SUBMISSION OF UNRESOLVED OBJECTIONS TO PETITIONER'S DEMONSTRATIVES has been served in its entirety by causing the aforementioned document to be electronically mailed to the following attorneys of record for the Petitioner listed below:

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Dated: November 5, 2024

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