

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.,
Petitioner

v.

10X GENOMICS, INC.,
Patent Owner

Case IPR2023-00958
Patent 10,697,013

**PATENT OWNER'S REQUEST UNDER 37 C.F.R. § 42.71(d) FOR
REHEARING OF THE BOARD'S FEBRUARY 5, 2024 DECISION
GRANTING PETITIONER'S REHEARING REQUEST AND
INSTITUTING *INTER PARTES* REVIEW**

LIST OF EXHIBITS

Exhibit	Description
EX2001	File History of U.S. App. No. 15/677,957
EX2002	File History of U.S. App. No. 13/859,450
EX2003	Dictionary of Microbiology and Molecular Biology (2d ed. 1987)
EX2004	File History of U.S. App. No. 14/792,094
EX2005	File History of U.S. App. No. 13/387,343
EX2006	U.S. Patent Pub. No. 2007/0238113
EX2007	Laird <i>et al.</i> , <i>Hairpin-bisulfite PCR: assessing epigenetic methylation patterns on complementary strands of individual DNA molecules</i> , 101 PNAS 204-09 (Dec. 12, 2003)
EX2008	Parse Biosciences, Inc. v. 10x, Genomics Inc., IPR2023-00876, Pap.1, (April 20, 2023)
EX2009	File History of U.S. App. No. 14/172,694
EX2010	Declaration of Sayem Osman

10x Genomics, Inc. (“PO”) hereby requests panel rehearing of the Board’s February 5, 2024 Decision Granting Petitioner’s Request on Rehearing of Decision Denying Institution of *Inter Partes Review* (Pap. 9 (“Decision”)) because, in granting institution, the Board overlooked several of PO’s arguments explaining how Petitioner failed to meet its burden to show obviousness of claim 1—the sole independent claim of U.S. Patent No. 10,697,013 (“’013”)—and, thus, every challenged claim. *See* 37 C.F.R. § 42.71(d).¹ More specifically, the Board overlooked arguments unique to ’013 (and not addressed in the POPRs for the related IPRs, IPR2023-00876 and IPR2023-00955) explaining why Petitioner’s obviousness argument failed to show that (or how) a second tag could be ligated to the TSO or CDS of Petitioner’s base reference, Linnarsson, while also practicing the rest of claim 1. *Compare* POPR, 53-57 (explaining why Petitioner’s obviousness combination involving ligating a second tag would fail to satisfy claim 1) *with* Decision, 16-19 (failing to address or acknowledge these substantive arguments regarding ligation).

The ’013 patent at issue here differs from the patents in related IPR2023-IPR2023-00876 and IPR2023-00955 because, *inter alia*, the sole independent

¹ Unless stated, statutory and regulatory citations are to 35 U.S.C. or 37 C.F.R., as context indicates, internal citations omitted, and emphases/annotations are added.

claim here requires **ligation** of a second tag. EX1001, cl.1.² The POPR here thus differed substantively from the POPRs in those proceedings because, here, PO has addressed certain reasons why modifying Linnarsson to add a second tag via ligation (as required for all '013 claims) would fail. POPR, 53-57.³ However, the Board overlooked those additional arguments from the POPR, instead largely tracking its reasoning from the two related petitions—focusing on whether McCloskey's tag might perform the function of the claimed second tag, and

² In contrast, the ligation requirement in the patents involved in IPR2023-00876 and IPR2023-00955 (U.S. Patent Nos. 10,155,981 and 10,240,197) is found only in a single dependent claim of each of those patents, and was either not addressed (in IPR2023-00876) or not addressed to the same extent (in IPR2023-00955).

³ In the instituted IPR2023-00876 proceeding, PO has provided additional explanation and argument in its POR as to why any such ligation would fail and provided additional evidentiary support through, *e.g.*, its expert, Dr. Quackenbush. IPR2023-00876, Pap. 13, 52-65 & EX2013, ¶¶ 89-104. If the Board were to deny PO's present request, PO would similarly offer further argument and evidence here. But even on this preliminary record with a limited set of arguments, Petitioner's arguments plainly fail for the reasons that PO identified but that the Board overlooked.

ignoring the POPR arguments describing why ligation would fail. For this reason, the Board should grant rehearing of its Decision Granting Petitioner's Request on Rehearing of Decision Denying Institution of *Inter Partes* Review and deny institution of this proceeding.

First—even assuming, consistent with the Board's Decision, that the tagged polynucleotide were to include a second tag ligated to the end of the CDS or TSO after extension (Decision, 14-15 (citing Pet.39))—the Decision ignored PO's argument that Petitioner failed to show how the entirety of any tagged polynucleotide resulting from Petitioner's proposed combination could then be ***amplified***, as claim 1 requires. EX1001, cl.1 ("amplifying said tagged polynucleotide, thereby generating a plurality of amplified polynucleotides corresponding to the tagged polynucleotide"). The POPR argued: "Petitioner also fails to explain how its combination would result in the claimed 'tagged polynucleotide,' which must then be amplified, if McCloskey's alleged tag were added to the *end* of Linnarsson's disclosed polynucleotide." POPR, 53.⁴ The POPR explained that Linnarsson's tagged polynucleotides have primers on the 5'

⁴ The end of the portion of the extended polynucleotide corresponding to the TSO or CDS is at the end of the polynucleotide. Pet.17-22; POPR, 7-8, 53-54; EX1003, 5:28-6:12, Fig. 11.

ends and their tags “are located *inside* the primer sequence... not on the *end* of a tagged polynucleotide.” POPR, 54-55. Indeed, Linnarsson’s disclosures only show amplification of the DNA *inside* the primers. *E.g.*, EX1003, 6:2-3, Fig.11. But Petitioner’s combination, to the extent it can, *arguendo*, be understood consistent with the Board’s Decision here (Pet.37-39), would ligate any second tag to the CDS or TSO, on the *outside* of the primers. Decision, 17-18. The POPR explains, “Petitioner does not address the significance of a ***primer*** not being on the 5’ end of the tag” or “explain how replication of the tag sequence would work (or even if it could work) if a ‘tag’ (rather than, *e.g.*, a primer) is at the end of the polynucleotide [*i.e.*, outside the primers of the CDS or TSO].” Pet.53-55. In other words, Petitioner never explained how, in its argument, the second tag would be amplified, as required by claim 1, when there was no primer on the outside of that tag sequence. *Id.* Thus, the Petition fails to meet its burden for this reason, and the Decision failed to address or acknowledge this POPR argument.

Second, even if a tagged polynucleotide, including a second tag, could, *arguendo*, be amplified in Petitioner’s proposed combination, the Decision also ignored PO’s argument that Petitioner failed to show how a second tag ligated to a TSO could be ***sequenced*** as required by claim 1(d). POPR, 55. According to the Board’s interpretation of Petitioner’s theory, the second tag would be ligated to the end of the TSO after extension, which would be on the 5’ end of any tagged

polynucleotide. Decision, 14-15 (citing Pet.39). The POPR explained:

“Linnarsson has a Bts sequence between the cell tag and the end of the cDNA. EX1003, Fig.11.” POPR, 54-55. And, “[a]ccording to Linnarsson, any sequence towards the 5’ end of the Bts sequence will be **removed**—*i.e.*, ‘released by BtsCI digestion....’” prior to sequencing. POPR55. As the POPR explained, “Petitioner fails to address why the alleged tag would not be **cleaved off**” if any tag were “simply ligate[d] to the end” of the TSO, as it would be located on the 5’ end of the Bts sequence. POPR, 55. “Once cleaved, there would be no ‘second tag sequence’ on the tagged polynucleotide when sequenced, and thus no ability to distinguish among sample polynucleotides as required by the claims.” POPR, 55. The Petition fails to meet its burden for this separate reason, and again the Decision failed to address or acknowledge this argument.

Third, Petitioner failed to show that its proposed technique for ligating the second tag to Linnarsson based on Hug would work. POPR, 55-56; *Health Care Logistics, Inc. v. Kit Check, Inc.*, IPR2019-00385, Pap.7, 14-15 (June 3, 2019) (denying institution because petitioner failed to explain how to modify a reference to meet a limitation and why a POSITA would be motivated to do so); *see also* POPR, 49 (citing *John Crane, Inc. v. Finalrod IP, LLC*, IPR2016-01827, Pap.6, 13-14 (Jan. 31, 2017); *Personal Web Techs., LLC v. Apple, Inc.*, 848 F.3d 987, 994 (Fed. Cir. 2017) (reversing obviousness determination where there was no “clear,

evidence-supported account of the contemplated workings of the combination” which “is a prerequisite to adequately explaining and supporting a conclusion” of obviousness); *ActiveVideo Networks, Inc. v. Verizon Commc’ns, Inc.*, 694 F.3d 1312, 1327-28 (Fed. Cir. 2012) (affirming reversal of obviousness verdict where expert “failed to explain how specific references could be combined” including “how any specific combination would operate or read on the asserted claims”); *Axon Enter., Inc. v. Digital Ally, Inc.*, IPR2017-00515, Pap.10, 18-19 (July 6, 2017) (denying institution, stating neither petitioner nor its expert “explains in sufficient detail the nature of Petitioner’s proposed modification... Petitioner does not explain in sufficient detail how the proposed modification is supposed to work”)). And Petitioner provided no other explanation for how the alleged ligation would occur using any other ligation technique. Pet.38-39. As the POPR explained:

Hug describes cutting double-stranded DNA with a particular restriction enzyme, resulting in double-stranded DNA with a 5’ sticky end with a particular overhanging sequence, and then adding short linkers. EX1007, 7-8, Fig.3. But unlike tags that distinguish polynucleotides (EX1001, cl.1), ***Hug’s linkers are not unique.*** Instead, the linkers consist of the recognition site of a restriction enzyme (a sequence that hybridizes to the sticky end resulting from cutting the DNA in the sample with a particular restriction enzyme, such as BamH1) and an end with a short polynucleotide sequence that

hybridizes to the other linker. EX1007, 7-8, Fig.3. Petitioner never acknowledges these conflicting details of Hug's ligation method, let alone explains how to use Hug's technique to ligate a "second tag" to the combination of Linnarsson and McCloskey, or what further modifications would be necessary to achieve ligation.

Pet.56. The Petition fails to meet its burden for these separate reasons, and again the Decision failed to address or acknowledge these arguments.

Fourth, the Decision also took no notice of PO's argument that "Petitioner ignores the biotin group at the 5' end of the CDS (Pet.32; EX1003, Fig.11), and fails to address how this would impact ligation, or how adding a tag *without* a biotin group on the end [resulting in a polynucleotide unlike Linnarsson's, which does have a biotin on the end] would impact Linnarsson's method. Pet.37-39, 32-33; EX1003, 32:18-25." POPR, 56-57. Indeed, the Petition never even mentions biotin in arguing the obviousness of claim 1. *See* POPR, 56-57. The Petition also fails to meet its burden for these separate reasons, and again the Decision failed to address or acknowledge these arguments.

Each of these overlooked POPR arguments assumed, *arguendo*, that (1) POSITA would have been motivated to combine Linnarsson and McCloskey, and (2) Petitioner's arguments could be understood—and thus each provides a further, independent reason that Petitioner's combination fails to render any '013 claim obvious. PO respectfully requests that the Board grant rehearing, consider these

arguments, and deny institution on this basis.

Respectfully submitted by:

Dated: February 15, 2024

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CERTIFICATE OF PAGE COUNT

The undersigned certifies that the foregoing PATENT OWNER'S
REHEARING REQUEST OF THE BOARD'S DECISION GRANTING
PETITIONER'S REQUEST ON REHEARING OF DECISION DENYING
INSTITUTION OF INTER PARTES REVIEW UNDER 37 C.F.R. § 42.71(d)
complies with the 15-page limitation in 37 C.F.R. §42.24(a)(1)(v).

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of PATENT OWNER'S REQUEST FOR REHEARING 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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