

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PARSE BIOSCIENCES, INC.,
Petitioner,

v.

10X GENOMICS, INC.,
Patent Owner.

Case No. IPR2023-00876
U.S. Patent No. 10,155,981

PETITIONER'S MOTION TO EXCLUDE

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I. INTRODUCTION

Pursuant to FRE 401, 402, and 403, Petitioner moves to exclude Exhibit 2101 and all arguments in Patent Owner’s Sur-Reply (Paper 26) (“POSR”) that rely upon or relate to Exhibit 2101. *See, e.g.*, POSR at 9-11. This evidence and argument all pertains to a restriction enzyme known as BtsI, which is a different enzyme than the BtsCI enzyme that is actually used in the Linnarsson prior art reference. Patent Owner’s arguments about the BtsI enzyme are thus irrelevant and prejudicial and, unfortunately, appear intentionally aimed to confuse the Board by capitalizing on the similar names “BtsI” and “BtsCI,” which differ by only a single letter.

Briefly, after Petitioner pointed out that Figures 3 and 4 of Linnarsson include neither a restriction enzyme site nor a biotin for use with the fragmentation and capture approach of Figure 11, Patent Owner apparently discovered that, by coincidence, Figures 3 and Figure 4 have a sequence for the BtsI restriction enzyme. Patent Owner then belatedly introduced extrinsic evidence to this effect during the cross-examination of Petitioner’s expert. *See* Exhibit 2101; POSR at 9-11.

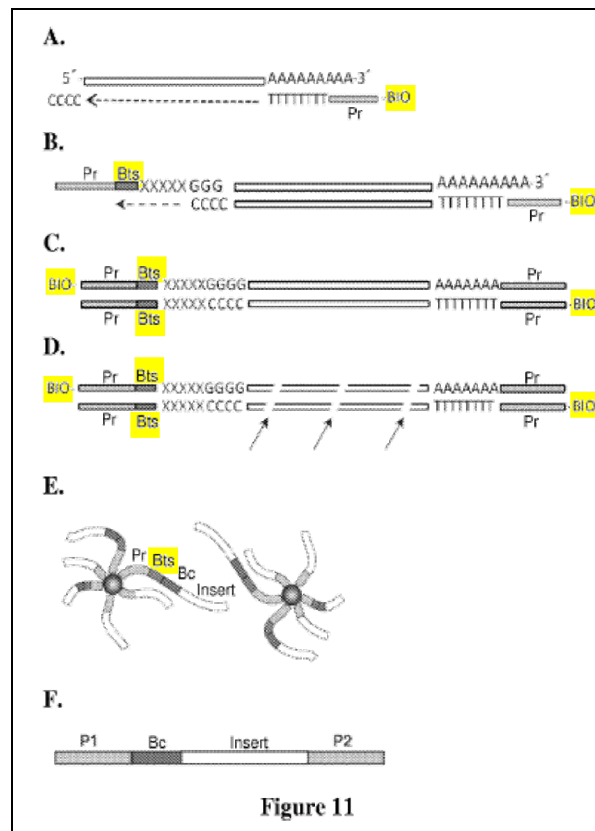
But neither the BtsI enzyme nor its associated cut sequence is ever called out or used anywhere in Linnarsson, let alone in Figure 11. Linnarsson uses a different enzyme—BtsCI. Patent Owner now tries to rely upon the coincidental appearance of a sequence for an enzyme *different* from the one Linnarsson actually uses to suggest that the fragmentation and capture approach in Figure 11 is also part of

Figures 3 and 4 of Linnarsson. This, however, is false, and is an attempt by Petitioner to confuse the Board by exploiting a coincidence and a similarity in the names of two *different* enzymes.

Patent Owner's new evidence about the BtsI enzyme is irrelevant and prejudicial and confuses the issues. It should be excluded.

II. BACKGROUND

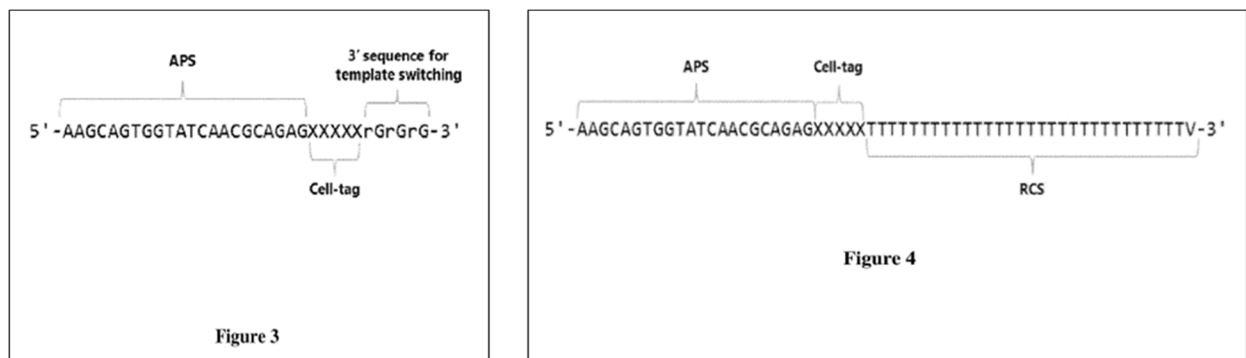
Patent Owner argued at length both in its response to the Petition and in its sur-reply that all embodiments of Linnarsson *required* an approach based on fragmentation and capture, which uses both a restriction enzyme and a biotin and that is set forth in Figure 11. *See, e.g.*, POR at 55 n.21; POSR at 9-11. This approach uses a restriction enzyme known as BtsCI, which recognizes a cut site that Linnarsson abbreviates as “Bts” and that has the nucleic acid sequence GGATG. *See, e.g.*, EX1003.007 (“Panel E shows an immobilization and end-repair step. Both 5' (with barcode (Br) and BtsCI site (Bts))....”); EX1064.001. Figure 11 of Linnarsson specifically identifies both the cut site and the biotin for use with this approach:



EX1003.0060 (highlighted annotations added). Patent Owner argued that this fragmentation and capture approach as in Figure 11 above was incompatible with Petitioner’s proposed combination of Linnarsson with McCloskey. *See* POR at 52-67. These alleged incompatibilities are one of Patent Owner’s key arguments against obviousness. *See id.*

As Petitioner pointed out, however, Patent Owner’s argument that aspects of Figure 11—including the biotin and Bts cut site—are mandatory is belied by Linnarsson itself, which says that Figure 11 discloses “steps *optionally used* in the STRT method.” EX1003.006 at 5:28-29 (emphasis added); *see also* EX1059 ¶¶ 66, 68; POSR at 9-10. Likewise, as Petitioner explained in its reply, Linnarsson

has embodiments in Figures 3 and 4 that use neither the Bts cut site nor the biotin. *See* Reply at 5-7. Unlike Figure 11, these figures do not refer to or include the Bts cut site or the biotin:



EX1003.052-053; EX1059 ¶¶ 36-42, 66-68. Patent Owner’s argument that Linnarsson requires fragmentation and capture as in Figure 11 is thus wrong.

Attempting to nonetheless salvage its fragmentation and capture argument, Patent Owner apparently scoured the Internet to find out whether the sequences in Figures 3 and 4 of Linnarsson happened to have ***any*** restriction enzyme sequence whatsoever, regardless of whether it was the cut site for the BtsCI enzyme actually used in Linnarsson. By sheer coincidence, Patent Owner discovered that the sequences above happen to include a sequence (*i.e.*, GCAGTG¹) corresponding to the cut site for the BtsI enzyme. Though having a name similar to BtsCI, the BtsI

¹ Petitioner notes that a typo appears in the BtsI sequence in the POSR: “restriction enzyme cut site (CGAGTG) that is present in Figs.3-4.” POSR at 10 (emphasis added). In fact, the cut sequence for BtsI is GCAGTG.

enzyme is a different enzyme that is neither used nor mentioned in Linnarsson. Not even once.

Nevertheless, in its cross-examination of Petitioner's expert, Dr. Gregory Cooper, Patent Owner introduced for the first time a scientific publication identifying the restriction enzyme cut site for BtsI. *See* EX2101. It then attempted to establish based on this evidence that Dr. Cooper was incorrect in asserting that Figures 3 and 4 do not use the capture and fragmentation approach in Figure 11. EX2020 at 133:19-137:6 *see also id.* at 123:20-127:12 (Dr. Cooper explains on cross-examination that BtsI and BtsCI are different enzymes and that the former is not used in Linnarsson). In its POSR, Patent Owner continued to suggest that because Figures 3 and 4 happened to include *a* restriction enzyme cut site—albeit not for the enzyme used in Linnarsson—that all embodiments of Linnarsson use fragmentation and capture as in Figure 11. *See, e.g.*, POSR at 9-11. Notably, Patent Owner makes this argument even though Figures 3 and 4 undeniably include no biotin, which is part-and-parcel for the approach of Figure 11.

III. ARGUMENT

“Irrelevant evidence is not admissible.” Fed. R. Evid. 402. Further, even to the extent evidence is relevant, the “court may exclude relevant evidence if its probative value is substantially outweighed by a danger of...unfair prejudice [or] confusing the issues....” Fed. R. Evid. 403.

Any evidence about the BtsI enzyme or its associated cut sequence is wholly irrelevant to the issues here. This is because, as documented above, the BtsI enzyme is not used or mentioned in Linnarsson. Even to the extent Figures 3 and 4 of Linnarsson coincidentally happen to include the cut sequence for the BtsI restriction enzyme, none of the protocols in Linnarsson use this sequence for anything, let alone the capture and fragmentation approach of Figure 11. Indeed, the Figure 11 method requires biotin, which is undisputedly absent from Figures 3 and 4 of Linnarsson. It thus cannot be that the unmentioned and undiscussed BtsI restriction enzyme sequence that, by pure happenstance, appears in Figures 3 and 4 is intended to be used for this approach.

In addition to being irrelevant, Patent Owner's new evidence regarding BtsI is prejudicial and confusing. The only restriction enzyme used in Linnarsson is BtsCI. *See* EX1003.007 (referring solely to BtsCI); EX1003.024 (disclosing protocols that use BtsCI); EX1003.031-032 (same); EX1003.036-037 (referring solely to BtsCI). BtsI is a different enzyme with a different cut sequence. By pointing to evidence about a restriction enzyme that is never mentioned in Linnarsson (BtsI) but that happens to have a name highly similar to the enzyme that is used in Linnarsson (BtsCI), Patent Owner seemingly aims to confuse the Board.

Indeed, to amplify the confusion, Patent Owner refers to the "Bts restriction site" in its POSR when referring to the BtsI cut site sequence. POSR at 10. As

documented above, however, “Bts,” is the abbreviation used in Linnarsson to identify the BtsCI restriction enzyme cut site that is used in Figure 11. *See, e.g.*, EX1003.007; EX1003.0060 (Fig. 11). In Linnarsson, the term “Bts” has nothing to do with the BtsI enzyme. Patent Owner’s attempt to nonetheless exploit the similarity in the names “BtsI” and “BtsCI” to mischaracterize the teachings of Linnarsson is the classic type of evidence and argument that ought to be excluded under Rule 403.

IV. CONCLUSION

Exhibit 2101 and all arguments in the Patent Owner’s Sur-Reply (Paper 26) that rely on Exhibit 2101 should be excluded.

Dated: June 21, 2024

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing **PETITIONER'S MOTION TO EXCLUDE** is being served on June 21, 2024, via electronic mail pursuant to 37 C.F.R. § 42.6(e) to the counsel for Patent Owner at the addresses below:

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