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. IPR2023-00955
U.S. Patent No. 10,240,197

---

**PETITIONER'S MOTION TO EXCLUDE**

## TABLE OF CONTENTS

**Page**

I. INTRODUCTION ..... 1

II. BACKGROUND ..... 2

III. ARGUMENT ..... 8

IV. CONCLUSION ..... 9

## TABLE OF AUTHORITIES

**Page(s)**

**Rules**

Fed. R. Evid. 401 .....1
Fed. R. Evid. 402 .....1, 8
Fed. R. Evid. 403 .....1, 8

## I. INTRODUCTION

Pursuant to FRE 401, 402, and 403, Petitioner moves to exclude all arguments in Patent Owner's Sur-Reply (Paper 31) ("POSR") that pertain to a restriction enzyme known as BtsI. Petitioner's objections to these arguments were previously set forth in Petitioner's Objections to Evidence Under 37 C.F.R. § 42.64. *See* Paper 33 at 2 (objecting to arguments based upon use of other restriction enzymes (including BtsI) in Linnarsson under Federal Rules of Evidence 403).

The BtsI enzyme is a different enzyme than the Bts***C***I enzyme that is actually used in the Linnarsson prior art reference relied upon by Petitioner. *See, e.g.*, POSR at 5-8. 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, *see* Reply at 6, 23, Patent Owner apparently discovered that, by coincidence, Figures 3 and 4 have a sequence for the BtsI restriction enzyme. Patent Owner then argued that Figures 3 and 4 are compatible with Linnarsson's fragmentation and capture approach, based solely on the

coincidental presence of a nucleotides that happen to correspond to the BtsI restriction enzyme sequence. POSR at 5-8.

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's attempt 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 is without merit. This is a mischaracterization of Linnarsson and 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 56; POSR at 5-9. 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))….”); EX1080.001. Figure 11 of Linnarsson specifically identifies both the cut site and the biotin for use with this approach:

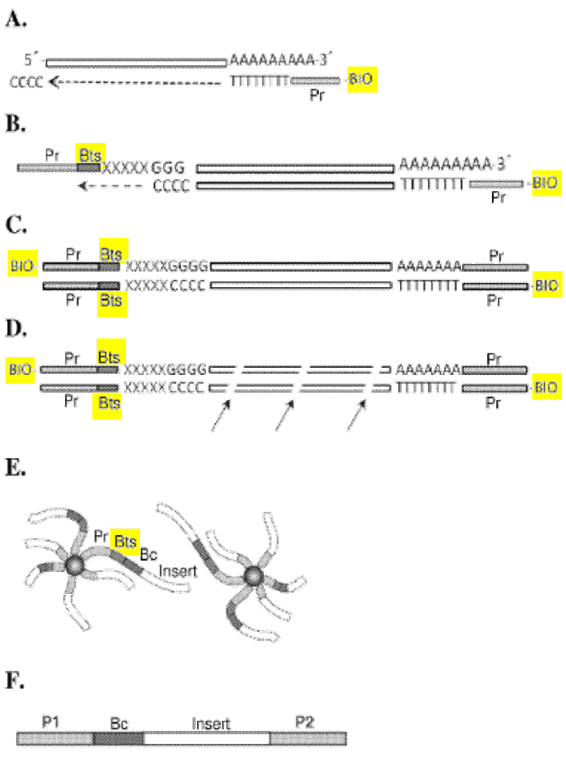


Figure 11

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 52-58. 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* EX1070 ¶¶ 96-99; POSR at 5-8. 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 6-8. Unlike Figure 11, these figures do not refer to or include the Bts cut site or the biotin:

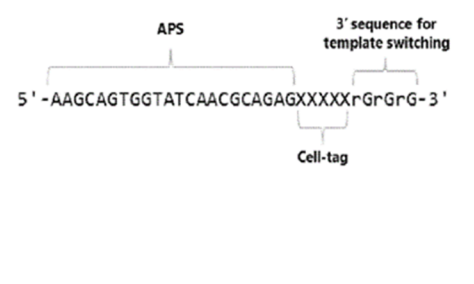



Figure 3

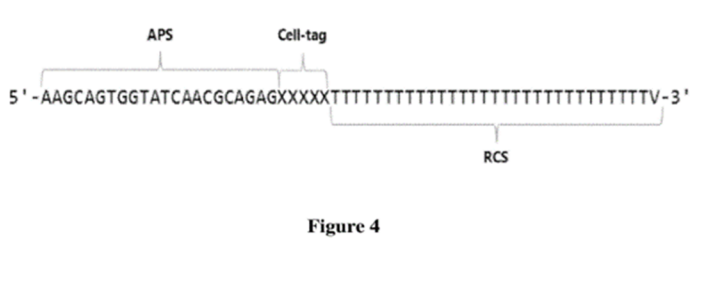



Figure 4

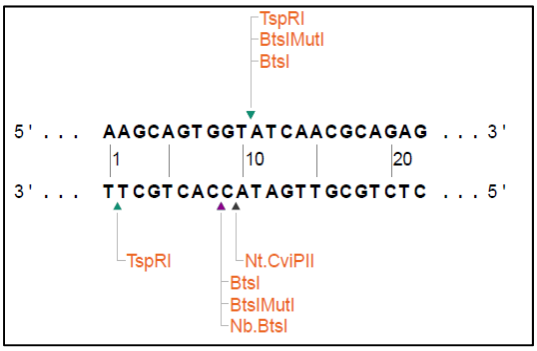
EX1003.052-053; EX1070 ¶¶ 44-50, 96-99. Patent Owner's argument that Linnarsson requires fragmentation and capture as in Figure 11 is thus wrong.

In an attempt to salvage its fragmentation and capture argument,[1] Patent Owner apparently scoured the Internet to find out whether the sequences in Figures

[1] In related IPR2023-00876, Patent Owner had belatedly introduced evidence on BtsI restriction enzyme in its sur-reply and argued that Figures 3 and 4 are subject to the fragmentation and capture approach. Petitioner had filed a motion to exclude this evidence. The Board in its Final Written Decision noted, "Petitioner's Motion to Exclude seeks exclusion of Exhibit 2101. As we do not rely on Exhibit 2101, Petitioner's Motion to Exclude is dismissed as moot." *Parse Biosciences, Inc. v. 10x Genomics, Inc.,* No. IPR2023-00876, Paper 47 at 2 (September 17, 2024).

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. Coincidentally, Patent Owner discovered that the sequences above happen to include a sequence (*i.e.*, GCAGTG[2]) corresponding to the cut site for the BtsI enzyme. Though having a name similar to BtsCI, the BtsI enzyme is a different enzyme that is neither used nor mentioned in Linnarsson. Not even once.

As Petitioner and Dr. Cooper explained, the presence of the BtsI sequence in Figures 3 and 4 is irrelevant. Reply at n.4; EX1070 at ¶¶57-58. In the words of Patent Owner's own expert, there are "probably tens of thousands of restriction enzymes" that can be "easily found" on the internet. EX1069 at 22:6-24:6. In fact, analysis of the relevant sequence from Figure 3 shows that it happens to include cut sequences for numerous different restriction enzymes:




| Select All | Enzyme | Recognition Sequence |
|---|---|---|
| | BtsI-v2 | GCAGTG NN |
| | BtsIMutI | CAGTG NN |
| | Nb.BtsI | GCAGTG |
| | Nt.CviPII | CCD |
| | TspRI | NNCASTGNN |

[2] Petitioner notes that a typo appears in the BtsI sequence in the POSR: "restriction enzyme cut site (***CG***AGTG) is present in Figs.3-4." POSR at 6 (emphasis added). In fact, the cut sequence for BtsI is GCAGTG.

EX1073. Despite this evidence, Patent Owner now decontextualizes Dr. Cooper's testimony to suggest that Figures 3 and 4 are subject to the fragmentation and capture approach in Linnarsson. POSR at 5-7.

Specifically, Patent Owner relies on Dr. Cooper's testimony (EX2040) to argue that Dr. Cooper "doesn't dispute another restriction enzyme cut site (CGAGTG) is present in Figs.3-4, and agrees POSITA would not interpret Linnarsson as limited to using only BtsCI." *Id*. at 6. It then argues that "[g]iven these ***admissions*** and Linnarsson's consistent disclosures of using biotin and fragmentation, Petitioner failed to show Figs.3-4 teach ***anything other than*** polynucleotide sequences for a compatible CDS (to which a biotin molecule would be added) and TSO for Ex. I's method." *Id.* at 6-7. It further attempts to establish that this testimony of Dr. Cooper contradicts his prior testimony wherein he testified that fragmentation is optional due to the lack of the restriction enzyme cut site in Figures 3 and 4. *Id.* at n.5.

Dr. Cooper, however, nowhere "admits" that Linnarsson contemplates the use of "another restriction enzyme cut site (GCAGTG) [sic]" or BtsI in Linnarsson including in Figures 3 and 4. On the contrary, Dr. Cooper affirms that the presence of BtsI in Figures 3 and 4 is "totally happenstance or coincidental:"

> **Q** What is your understanding of whether Linnarsson is contemplating use the Bts-1 restriction enzyme with any of its approaches?

> **A** It is – Bts-1 isn't mentioned. ***That's a different enzyme than the one that is part of the example in Linnarsson***.

EX2040 at 70:14-22 (objection omitted)

> **Q** Okay. What's your understanding of whether Linnarsson ever refers to those sequences of nucleotides that happen to correspond to the Bts-1 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***.

*Id.* at 71:10-21 (objection omitted)

Dr. Cooper's testimony (EX2040) is further consistent with its prior testimony that fragmentation is optional due to the lack of the restriction enzyme cut site in Figures 3 and 4, contrary to what Patent Owner alleges:

> **Q** What's your understanding of whether Figures 3 and 4 include a restriction enzyme cut site for use with the fragmentation and capture approaches that are disclosed in Linnarsson?
>
> **A** I don't believe they include that, because the portions of the molecule that are depicted in Figures 3 and 4 are all demarcated with whether it's part of the priming site, part of the cell tag, et cetera. So there's not an allocation to a cut site.

*Id.* at 69:18-70:5; *see also id.* at 37:5-10 ("And so ***Linnarsson certainly encompasses a range of protocols, some of which wouldn't use restriction enzymes at all***, for example.").

In its POSR, however, Patent Owner continues to suggest that because Dr. Cooper did not dispute that 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 5-8. 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 or arguments 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. EX2040 at 71:10-21.

In addition to being irrelevant, Patent Owner's arguments 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 arguing 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. This the classic type of evidence and argument that ought to be excluded under Rule 403.

## IV. CONCLUSION

For these reasons, all arguments in the Patent Owner's Sur-Reply (Paper 31) on the BtsI enzyme should be excluded.

Dated: October 11, 2024

Respectfully submitted,

*/Derek C. Walter/*

Derek C. Walter
Lead Counsel for Petitioner
Reg. No. 74,656
Weil, Gotshal & Manges LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
derek.walter@weil.com

Adrian C. Percer
Reg. No. 46,986
Weil, Gotshal & Manges LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
adrian.percer@weil.com

William Sutton Ansley
Reg. No. 67,828
Weil, Gotshal & Manges LLP
2001 M Street NW, Suite 600
Washington, DC 20036
sutton.ansley@weil.com

Edward R. Reines
(*Pro Hac Vice*)
Weil, Gotshal & Manges LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
edward.reines@weil.com

## CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing **PETITIONER'S MOTION TO EXCLUDE** is being served on October 11, 2024, via electronic mail pursuant to 37 C.F.R. § 42.6(e) to the counsel for Patent Owner at the addresses below:

J. Steven Baughman (Reg. No. 47,414)
Megan Raymond (Reg. No. 72,997)
GROOMBRIDGE, WU, BAUGHMAN
& STONE LLP
801 17th Street, NW, Suite 1050
Washington, DC 20006
P: (202) 505-5832
steve.baughman@groombridgewu.com
megan.raymond@groombridgewu.com
10X-Parse-IPR@groombridgewu.com

*Counsel for Patent Owner*

Dated: October 11, 2024

By: */Derek C. Walter/*
Derek C. Walter
Lead Counsel for Petitioner
Reg. No. 74,656