

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC,
Petitioner,

v.

NANOSTRING TECHNOLOGIES, INC.
Patent Owner

Case IPR2023-01300
U.S. Patent No. 11,473,142

PATENT OWNER'S PRE-INSTITUTION SUR-REPLY

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Patent Owner files this pre-institution Sur-Reply as authorized by the Board. EX3001, EX3005. In the Petition, 10x Genomics, Inc. (“Petitioner”) argued that both Stahl and So-456 teaches the “sequencing step” and “synthesis step” of claim 1 of the ’142 Patent. Patent Owner (“PO”) persuasively rebutted these contentions in its Patent Owner’s Preliminary Response (Paper 6, “POPR”). Rather than respond to these allegations on the substance, however, Petitioner presents on reply meritless allegations that PO has taken inconsistent positions in parallel litigation. Paper 7 (Petitioner’s Reply). This sur-reply addresses those allegations.

A. Petitioner fails to demonstrate inconsistencies regarding the “sequencing step”

Contrary to Petitioner’s contention, PO’s position is not that Stahl and So-456 do not teach the sequencing step solely “because their methods sequence products that are generated downstream of...the first cDNA products.” Paper 7 at 1. Instead, PO pointed out the deficiency in what *Petitioner* identified as the “DNA products” in Stahl and So-456 and why those particular “DNA products” were not sequenced as required.¹ See Paper 6 at 15-20, 28-33. As documented below,

¹ Claim 1(e) requires “identifying the first plurality of DNA products and the second plurality of DNA products synthesized in step (c) and step (d) by *sequencing the*

Petitioner incorrectly reframes PO's argument to avoid addressing the merits.

PO's infringement position in district court litigation is clear. PO pointed to specific DNA products in Visium Fresh-Frozen's workflow that are synthesized and sequenced. EX1022 at 18-20, 22-24. For example, PO pointed to steps 1 ("Permeabilization & Reverse Transcription") and 2 ("Second Strand Synthesis & Denaturation") for synthesizing the "DNA products"² and steps 4 ("Visium Spatial Gene Expression Library Construction") and 5 ("Sequencing") for sequencing the "DNA products." Petitioner does not dispute this. Paper 7 at 2-3.

Petitioner, however, rewrites PO's position such that any "DNA products that are generated downstream of the first cDNA products" are supposedly encompassed by claim 1. *Id.* at 3. That is neither PO's words nor position.

Nowhere does Petitioner dispute that it identified specific products in Stahl and So-456 as the synthesized "DNA products" and that these are not sequenced.

first plurality of DNA products and the second plurality of DNA products." See EX1043 at 147:54-57.

² Claims 1(c) and (d) require "synthesizing a [first/second] plurality of DNA products...." See EX1043 at 147:42:53.

See Paper 2 at 26-27, 61-62; *see also* Paper 6 at 16, 28-29. For Stahl, Petitioner identifies a cDNA strand reverse-transcribed from sample mRNA as the “DNA products” even while Stahl teaches sequencing amplified RNA molecules. *Id.* at 15-20. Similarly for So-456, Petitioner identifies a first strand cDNA as the “DNA products” while So-456 teaches sequencing a second strand cDNA. *Id.* at 28-33. Accordingly, PO’s position in this proceeding is simply that Petitioner has failed to meet its burden to show how Stahl and So-456 disclose the “sequencing step.” To the extent Petitioner now seeks to point to different products in Stahl and So-456 as the “DNA products,” it should be precluded from doing so. *See Koninklijke Philips N.V. v. Google LLC*, 948 F.3d 1330, 1335 (Fed. Cir. 2020) (citation omitted).

As such, Petitioner fails to identify inconsistent positions as to the “sequencing step” and does nothing more than broaden PO’s infringement contentions to one that PO did not make.

B. Petitioner fails to demonstrate an inconsistent position regarding the “synthesis step”

Petitioner likewise falls short when it alleges that the “synthesis step” of Stahl and So-456 is “the same type of synthesis reaction” performed by Visium Fresh-Frozen. *See* Paper 7 at 4. Specifically, Petitioner mischaracterizes PO’s infringement theory such that Stahl/So-456 is compared against *part* of PO’s

contentions while the rest is *ignored*. Petitioner’s argument is improper and incorrect—PO’s actual infringement contentions are not inconsistent with its position in the POPR.

PO’s infringement contentions for the claimed synthesis reaction that “incorporates at least one nucleic acid sequence that identifies the [] location of the tissue sample” specifically refer to *both* Visium Fresh-Frozen’s steps 1 and 2, as Petitioner admits. ’142 Patent Claim 1(c) and (d); *see* EX1022 at 18-20; Paper 7 at 4. Petitioner argues, however, that PO’s infringement position regarding step 2 should be ignored because it “cannot form the basis of PO’s infringement allegations.” *Id.* at 5 (“Visium FF’s Step 2...cannot form the basis of PO’s infringement allegations...Thus, PO’s infringement allegations...could only be based on Visium FF’s Step 1.”). Undisputedly, PO’s contention is that steps 1 and 2 *together* perform the claimed synthesis reaction. *See* EX1022 at 18-22; *see also* Paper 7 at 5 (Petitioner admitting that step 1 uses “the captured sample mRNA as a template” and step 2 incorporates the spatial barcode through a “second-strand synthesis”). Petitioner’s disagreement with PO’s district court infringement contentions is not a valid basis for rewriting PO’s position to argue that it is inconsistent with its position here. *See id.* at 5.

Importantly, Visium FF’s step 2 includes a “Second Strand Synthesis” that

proceeds along the sample sequence and capture probe to incorporate a spatial barcode. *See* EX1022 at 18-20. In contrast, as explained in the POPR, Stahl and So-456 do not disclose a synthesis reaction that incorporates the spatial barcode. Paper 6 at 21-25, 33-38. As Petitioner admits, the “type of synthesis reaction taught in Stahl and So-456” “uses the capture probe (comprising a spatial barcode) as a primer and the captured sample mRNA as a template, such that the first cDNA products from the synthesis reaction comprise a spatial barcode.” Paper 7 at 5. Thus, simply put, Visium FF incorporates the spatial barcode by synthesizing the spatial barcode while Stahl and So-456 teach an extension from the capture probe that *does not* incorporate the spatial barcode via a synthesis reaction.

Accordingly, Petitioner’s allegation of inconsistent positions as to the “synthesis step” is unfounded and appears to simply be an effort to dodge the substantive merits of PO’s arguments in the POPR by recasting its own arguments from what is set forth in its petition and rewriting PO’s infringement contentions.

Dated: July 8, 2024

Respectfully submitted,

/Derek C. Walter/

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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of **PATENT OWNER'S PRE-INSTITUTION SUR-REPLY** was served on **July 8, 2024**, via email pursuant to 37 C.F.R. and § 42.6(e) to the Petitioner at the addresses below:

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