

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner

v.

NANOSTRING TECHNOLOGIES, INC.,
Patent Owner

Case IPR2023-01298
U.S. Patent No. 11,377,689

PETITIONER'S PRE-INSTITUTION REPLY

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Patent Trial and Appeal Board
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Petitioner files this pre-institution Reply as authorized by the Board. Paper 9,

2. Patent Owner (“PO”) argues that paragraphs [252] and [261] of the 487 application describe an embodiment of the 689 patent’s claimed methods in which whole probes are collected. POPR, 37-39. PO’s argument—which is bare attorney argument not supported by expert testimony¹—mischaracterizes these disclosures because neither paragraph describes collecting whole probes and using them in subsequent steps, *as claimed*.

PO argues that paragraphs [252] and [261] describe “certain embodiments wherein the entire ‘intact probe’ is collected.” POPR, 37-39; EX1009, ¶¶[252], [261]. This is incorrect because the so-called collection in paragraph [252] is *not* a “collecting” step, as claimed. The claimed methods require using the collected “nucleic acid [and ligated] probes, or portions thereof” in the subsequent extension steps of claim 1(d)-1(e) and claim 16(e)-16(f) to spatially detect a target analyte. Contrary to the requirements of the claims, paragraph [252] teaches only that intact

¹ In contrast, the Petition is fully supported by the expert testimony of Dr. Spellman. *See* Pet., 53-55; EX1002, ¶¶287-292; *Roku, Inc. v. Universal Elecs., Inc.*, IPR2021-00758, Paper 7, at 29 (P.T.A.B. September 27, 2021) (weighing Petitioner’s argument supported by expert testimony against Patent Owner’s bare attorney argument and finding that “[p]etitioner makes a sufficient showing”).

probes can be removed and discarded through “a negative purification” to reduce “[b]ackground noise”—neither paragraph [252] nor paragraph [261] nor any other paragraph in the 487 application describes collecting intact probes for use in the subsequent claimed method steps to spatially detect a target analyte.

Paragraph [252] explicitly states: “*Background noise*, during nucleic acid detection, *can be reduced* by performing a *negative purification* of the *intact probe* molecule.” EX1009, ¶[252] (emphasis added). It characterizes the “intact probe[s]” as undesirable contaminants responsible for background noise. It further discloses that this background noise can be reduced by “negative purification of the intact probe molecule[s],” *i.e., removal of the unwanted intact probes*. EX1009, ¶[252]. PO admits this disclosure refers to “background noise.” POPR, 38.

Paragraph [252] also discloses that negative purification can be performed by “conducting an affinity purification” of the intact probes’ “target binding domain or photo-cleavable linker,” and states that the “released signal oligonucleotides will *not* be pulled out of solution” during negative purification. EX1009, ¶[252] (emphasis added). Thus, during the negative purification, the released signal oligonucleotides (*i.e., the cleaved identifier oligonucleotide portions of probes*) are not pulled out; they are retained in the eluate for the subsequent spatial detection steps of the claims. Meanwhile, the “intact probe[s]” are *pulled out* and discarded to reduce undesirable background noise. *Id.*

Paragraph [252]’s disclosure of reducing “background noise” by “performing a negative purification” to remove and discard “intact probe[s]” that might be present is not a description of “collecting” whole probes as claimed. The claimed methods require using the collected “nucleic acid [and ligated] probes, or portions thereof” in the subsequent extension steps of claims 1(d)-1(e) and 16(e)-16(f). The claims require that the extension reaction “incorporates at least one nucleic acid sequence that identifies the first [and second] location of the tissue sample into each of the nucleic acid [and ligated] *probes, or portions thereof collected in [the preceding steps].*” EX1001, 146:53-147:4, 148:23-40 (emphasis added). The claimed extension steps do not use the contaminating “intact probe[s]” of paragraph [252] (which were already removed) to spatially detect any analyte.

The 487 application lacks any description of using these contaminating “intact probe[s]” in its spatial detection methods. PO relies on paragraph [261] of the 487 application to argue that “these collected ‘intact probes’ can be used to detect target analytes.” POPR, 39. But paragraph [261] provides no details on the probes used in the claimed methods, let alone whole probes. EX1009, ¶[261]. “[A]dequate written description does not ask what is permissible, rather, it asks what is disclosed.” *D Three Enters., LLC v. SunModo Corp.*, 890 F.3d 1042, 1052 (Fed. Cir. 2018). The 689 patent is therefore not entitled to any of its claimed priority dates. *Id.* The Board should reject PO’s arguments and institute this IPR.

Respectfully submitted,

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CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

I certify that the above-captioned **PETITIONER'S PRE-INSTITUTION
REPLY** was served in its entirety on December 15, 2023, upon the following
parties via electronic mail:

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