

UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

FORESIGHT DIAGNOSTICS INC.,
Petitioner,

v.

PERSONALIS, INC.,
Patent Owner.

IPR2023-00224
U.S. Patent No. 11,384,394

**PETITIONER'S AUTHORIZED RESPONSE
TO PATENT OWNER'S NEW SUR-REPLY
EVIDENCE AND ARGUMENTS**

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Chicago Manual of Style (EX2178): EX1216 puts “capture” in quotes to highlight it as a scientific term, after stating in the preceding sentence, without the use of quotes, that “[t]he major differences with all the platforms [including “traditional multiplex PCR”] are the way in which *multiple loci are captured and amplified.*” EX1216.1. “[O]ligo-probes,” i.e., hybrid capture baits, are then listed as a quote/unquote “capture” mechanism right after PCR. *Id.* See also EX1220 at 24:2-4 (Personalis Executive describing pulldown probes having “a physical, often referred to as a, *quote/unquote*, pull-down that occurs.”).

Dudley 2021 (EX2181): There is no dispute that PCR primers comprise “a nucleic acid sequence that hybridizes to target DNA...in solution,” and Personalis’s witnesses confirmed that they “can physically capture and isolate the target DNA.” Reply 12-13. Thus, PCR primers satisfy even Personalis’s (incorrect) construction. Personalis responded that “Foresight has no reply to” (new exhibit) EX2181’s statement that “hybrid capture-based workflows” can take longer than PCR (days instead of hours)¹ and can be more expensive. Sur-Reply 8. This is a strawman: there is no dispute that there are different types of capture probes and that each may have pros and cons in certain situations, none

¹ Such timing differences are immaterial to the claims. See e.g., EX1002, Fig. 4. Indeed, delays for materials to be shipped are not uncommon. See EX1220 at 18:17-23:1.

of which are recited in the claims. Moreover, none of the considerations mentioned in 2021 by EX2181 – which emphasizes the overlapping applicability of PCR capture probes (referencing Forshew) and hybrid capture baits (referencing Newman) for MRD detection and tumor genotyping of various types of polymorphisms – teach away from using either approach. EX2181.201.

Leary 2012 (EX2183): Multiple examples from the contemporaneous literature confirm that a POSA deemed Leary’s (EX1002) PARE technique to constitute “whole genome sequencing.” EX1225 ¶¶26-29. This is further confirmed by Personalis’s contemporaneous patents. *Id.* ¶¶22, 68. Personalis responds with the fallacious argument that because certain other non-exhaustive lists of WGS references do not include Leary 2010, then it must not be WGS.

First, Personalis argued that Meyerson “specifically exclude[d] Leary from WGS.” POR 9. The Reply established that Personalis’s characterization was inaccurate, because Meyerson listed McBride’s substantially similar technique as WGS. EX1225, ¶¶25-27. In Sur-Reply, Personalis had no response.

Next, Personalis contended that “Foresight’s founders reviewed WGS references and specifically did not classify Leary as teaching WGS.” POR 9 (citing Newman, EX2152). But the “WGS references” Personalis flagged were in actuality “focused on measurements on ctDNA,” and the “part [Dr. Furneaux] bolded cites four studies regarding the whole genome sequencing of ctDNA.”

Ex1225, ¶¶29-31. Again, Personalis had no substantive response, though it redoubled its inaccurate assertion that “Foresight’s Founders...excluded Leary from their lists of WGS references.” Sur-Reply 8.

One of the references that Dr. Furneaux bolded as a WGS reference was Leary 2012. EX2152.11 (Reference 9). To correct Personalis’s misleading assertion that Newman had a list of “WGS references” (as opposed to WGS *ctDNA* references), Dr. Quackenbush pointed to Newman’s focus on WGS of ctDNA, along with Leary 2012’s title, “Detection of Chromosomal Alterations *in the Circulation* of Cancer Patients with Whole-Genome Sequencing,” which is recited in Newman’s bibliography. EX1225, ¶32.

In its sur-reply, Personalis argued that, since Leary’s authors used the term WGS in 2012 (EX2183) but not in Leary 2010 (EX1002), then EX1002 must not have used WGS. Sur-Reply 9. Personalis introduced EX2183 at Dr. Quackenbush’s deposition, but did not cite any of his testimony on it. As he testified, the Leary 2012 authors are “not replacing PARE with whole genome sequencing. They’re replacing digital PCR with PARE, which is whole genome sequencing. So I think you’ve got the interpretation of this kind of backward.” EX2188, 216:4-10; *id.* at 217:10-20; EX2183, Abstract (describing “Whole-genome analyses of DNA *from the plasma*”).

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify, pursuant to 37 C.F.R. section 42.6, that on February 29, 2024, that a complete copy of the foregoing document is being served via electronic mail upon:

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