

Paper No. _____
Filed: January 2, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Petitioner,

v.

THE CHINESE UNIVERSITY OF HONG
KONG,
Patent Owner.

Case No. IPR2024-00028
Patent No. 11,091,794

PETITIONER'S MOTION TO EXCLUDE
37 C.F.R. §42.64(c)

I. INTRODUCTION

Petitioner (PacBio) respectfully requests exclusion of Patent Owner (PO)'s exhibits 2002 and 2041 for violation of the Federal Rules of Evidence (FRE).

Exhibit 2041 is the second, or “supplemental,” declaration of Dr. Koo filed by Patent Owner together with its Patent Owner response. PacBio timely objected to EX2041. Paper 16, 1-2. Dr. Koo's testimony disregards both the broad scope of the challenged claims and more than half the evidentiary record, and his opinions are predicated on various legal and factual errors. Given the large volume of prior art references and petition materials not considered, Dr. Koo's proffered opinions are not relevant, cannot be of assistance to the Board as the trier of fact, and are not “the product of reliable principles” or methods “reliably applied” to the facts of this case. Dr. Koo is simply unable to testify as to the perspective of a POSA or offer rebuttal to a case he didn't assess critically or entirety. As such, EX2041 should be excluded.

Exhibit 2002 is the first declaration of Dr. Koo, which was filed with Patent Owner's Preliminary Response. PacBio timely objected to EX2002. Paper 11, 1-2. EX2002 was not relied upon in Patent Owner's post-institution briefing and is therefore irrelevant and unavailable to support Patent Owner's rebuttal case. In addition, EX2002 suffers from the same defects discussed herein with respect to Dr. Koo's second “supplemental” declaration (EX2041). To the extent EX2002 is

relevant, it is inconsistent with EX2041 and demonstrates the lack of credibility of Dr. Koo's testimony.

The extensive volume of disregarded evidence, inconsistencies, and errors both factual and legal should give the Board considerable pause before crediting any portion of Dr. Koo's testimony. Accordingly, both EX2041 and EX2002 should be excluded.

II. LEGAL STANDARD

The Federal Rules of Evidence (FRE) govern the admissibility of evidence submitted during an *inter partes* trial before the PTAB. 37 C.F.R. §42.62(a). The FRE govern admissibility of expert testimony. FRE 702 requires that a purported expert is sufficiently qualified by knowledge such that the testimony "will help the trier of fact to understand the evidence or to determine a fact in issue"; that "the testimony is based on sufficient facts or data"; that "the testimony is the product of reliable principles and methods"; and that "the expert has reliably applied the principles and methods to the facts of the case." Fed. R. Evid. §702. The proponent of expert testimony must demonstrate its admissibility by a preponderance of the evidence. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.W. 579, 592 n.10 (1993).

Under FRE 401, evidence is relevant only if "(a) it has any tendency to make a fact more or less probable than it would be without the evidence; and (b) the fact

is of consequence in determining the action.” Fed. R. Evid. §401. Irrelevant evidence is not admissible. Fed. R. Evid. §402. Under FRE 403, the Board may exclude even relevant evidence if its probative value is substantially outweighed by danger of unfair prejudice, confuses the issues, is misleading, or wastes time. Fed. R. Evid. §403.

Where a witness selectively and inexcusably fails to consider material aspects of the relevant record, the Board “may conclude that there is simply too great an analytical gap between the data and the opinion proffered.” *GE v. Joiner*, 522 U.S. 136, 146 (1997). “[W]hen an expert ‘fail[s] to take into account a plethora of specific facts’ his or her testimony is properly excluded.” *David E. Watson, P.C. v. United States*, 668 F.3d 1008, 1014 (8th Cir. 2012) (quoting *Neb. Plastics, Inc. v. Holland Colors Ams., Inc.*, 408 F.3d 410, 417 (8th Cir. 2005)); see also *SAS Inst., Inc. v. World Programming Ltd.*, 125 F. Supp. 3d 579, 590 (E.D.N.C. 2015) (citing *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 202 (4th Cir. 2001)) (Expert testimony should be excluded “where the expert cannot provide a reasoned basis for his failure to consider additional evidence.”).

Moreover, expert testimony is neither relevant nor reliable, and therefore inadmissible, when it is predicated on an erroneous legal standard. *VirnetX, Inc. v. Cisco Sys.*, 767 F.3d 1308, 1328 (Fed. Cir. 2014) (holding that “the district court should have exercised its gatekeeping authority” to exclude expert testimony

applying the wrong legal standard); *see also U.S. Gypsum Co. v. Lafarge N. Am. Inc.*, 670 F. Supp. 2d 737, 745 (N.D. Ill. 2009) (“Having applied the incorrect legal standard..., Davis will not be permitted to testify on that topic.”).

III. EX2041 – SUPPLEMENTAL (SECOND) PETER KOO DECLARATION

PacBio respectfully moves to exclude EX2041. Given the large volume of prior art references and petition materials not considered, Dr. Koo’s proffered opinions are not relevant, cannot be of assistance to the Board as the trier of fact and not “the product of reliable principles” or methods “reliably applied” to the facts of this case. FRE 702, 402, 403; *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589 (1993). A POSA “is presumed to be aware of all the pertinent prior art.” *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985). It is black letter law that section 103 requires consideration of both the of the challenged claims and full “the scope and content of the prior art.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Dr. Koo disregards both the broad scope of the challenged claims and more than half the evidentiary record. Moreover, Dr. Koo’s opinions are predicated on various legal and factual errors. Consequently, Dr. Koo is unable to testify as to the perspective of a POSA or offer rebuttal to a case he didn’t assess critically or entirety. As such, EX2041 should be excluded.

A. Dr. Koo Flatly Ignored More than Half the Record

As shown in the list of exhibits provided in the Petition, the petition

materials identify 44 different exhibits supporting the challenge, including the '794 patent itself and its file history.¹ These exhibits were cited to and discussed by Petitioner and PacBio's expert, Dr. Dessimoz. PacBio has identified, and Dr. Koo confirmed, that at least 25 exhibits were not considered by Dr. Koo in his declaration testimony. This includes at least the following references:

- EX1013 (Davis, Entering the Era of Bacterial Epigenomics with Single Molecule Real Time DNA Sequencing) – *See, e.g.*, Pet. 5.
- EX1017 (Zou, A Primer on Deep Learning in Genomics) – *See, e.g.*, Pet. 10-11, 33, 54.
- EX1018 (Clement, US2016/0326593) – *See, e.g.*, Pet. 13, 59-65.
- EX1019 (PacBio Template Guide) – *See, e.g.*, Pet. 13-14, 65-68.
- EX1020 (Tsai, US2016/0208241) – *See, e.g.*, Pet. 14, 68-72.
- EX1023 (Eid, Real-time DNA sequencing from single polymerase molecules) – *See, e.g.*, Pet. 4 n.1.
- EX1024 (Flusberg PCT) – *See, e.g.*, Pet. 69.
- EX1025 (Korlach, Single-Molecule Sequencing) – *See, e.g.*, Pet. 4.
- EX1027 (Schreiber, Error Rates for Nanopore Discrimination among

¹ Two further exhibits (EX1045 and EX1046) were submitted prior to institution pursuant to Board authorization.

Cytosine, Methylcytosine, and Hydroxymethylcytosine along Individual DNA Strands) – *See, e.g.*, Pet. 4.

- EX1028 (Langlotz) – *See, e.g.*, Pet. 10-11.
- EX1029 (Miotto, Deep Learning for Healthcare) – *See, e.g.*, EX1002, ¶44 (cited at Pet. 11).
- EX1031 (Ray) – *See, e.g.*, Pet. 10.
- EX1032 (Wenger) – *See, e.g.*, Pet. 10-11.
- EX1034 (Lau) – EX1002, ¶¶53-54 (discussing Lau) (cited at Pet. 12-13).
- EX1035 (Tahir) – *See, e.g.*, Pet. 4, 10-11, 33.
- EX1036 (DeepVariant Usage Guide) – *See, e.g.*, Pet. 10-11.
- EX1037 (18/189,084 File History) – *See, e.g.*, Pet. 28, 37.
- EX1039-EX1041 (authenticating declarations) – *See, e.g.*, Pet. 4, 12, 13-14.
- EX1042 (GitHub, PacBio BAM 3.0) – *See, e.g.*, Pet. 12.
- EX1043 (GitHub, PacBio BAM 5.0) – *See, e.g.*, Pet. 12.
- EX1044 (PacBio Sequencing – How it Works video file) – *See, e.g.*, Pet. 4 n.1.
- EX1045 (Flusberg-666, US11,844,666).
- EX1046 (US17/891,899 File History).

Dr. Koo confirmed, in both his direct and cross-examination testimony, that

his declaration did not take into consideration the 25 identified exhibits listed above. In his declaration, Dr. Koo identifies EX2032 and EX2055 as the list of references considered and forming the basis of his declaration opinions. EX2041, ¶9. None of the 25 references identified above are identified in EX2032 or EX2055. During cross-examination, Dr. Koo confirmed he had not considered any of the above identified 25 references from the petition materials. *See, e.g.*, EX1049, 19:4-8 (“Other than the references listed in Exhibit 2032 and Exhibit 2055, did you consider any other references in writing your second declaration? A. Not that I can recall.”); *see also id.*, 128:22-129:25 (confirming no consideration of Tahir (EX1035)), 140:5-23 (confirming no consideration of Wenger (EX1032), EX1019 (PacBio Template Guide), or EX1020 (Tsai)), 150:7-19 (confirming no consideration of EX1013 (Davis) or EX1018 (Clement)). Neither Dr. Koo nor Patent Owner explain why such an extensive portion of the record was withheld from Dr. Koo.

The above identified references are material to issues of unpatentability, including argument raised in the petition materials, and withholding them from Dr. Koo’s consideration undermines his declaration testimony as unreliable and irrelevant. As discussed above, a POSA is one who is “aware of all the pertinent prior art,” rather than one who is selectively uninformed. Moreover, analysis under §103 requires considering “the scope and content of the prior art,” not ignoring it.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007). But Dr. Koo does just that—he failed to consider scores of prior art references relevant to the petition challenge, many of which directly conflict with his declaration testimony.

For example, the Tahir reference (EX1035) was cited in the Petition but withheld for Dr. Koo's consideration and directly contradicts various aspects of his testimony. The primary argument advanced by Patent Owner and Dr. Koo is that the prior art allegedly taught away from including nucleotide identity as input data for methylation detection. While that argument fails for a variety of reasons, Tahir expressly discloses using nucleotide identity as the input matrix to a convolutional neural network (CNN) for the purpose of detecting methylation sites. EX1035, Fig. 1. Tahir even uses the same Keras CNN in the Tse paper. Dr. Koo parrots Patent Owner's litigation argument alleging "copying," stating that PacBio's primrose product and Tse's holistic kinetic (HK) model have "similarities" and "duplicative features." EX2041, ¶¶80-86. During cross-examination, however, Dr. Koo conceded that Tahir illustrates that the allegedly "similar" matrix "input layer," convolutional layers," and an "output layer based on a sigmoid function" are all just conventional prior art CNN structures—not evidence of non-obviousness. Compare EX2041, ¶85, with EX1049, 81:18-83:6; 129:3-135:23; see also, Reply 21-23. By withholding prior art references like Tahir, Dr. Koo repeats misleading and unreliable litigation arguments, not testimony that "will help the trier of fact to

understand the evidence or to determine a fact in issue.” FRE 702.

As additional examples, EX1018 (Clement), EX1019 (PacBio Template Guide), and EX1020 (Tsai) are specifically cited as grounds references in Grounds 2-4 of the petition but were not considered by Dr. Koo. While Patent Owner is permitted to concede challenges to dependent claims as uncontested, the cited references are still part of the scope and content of relevant prior art that a POSA would consider. These references were not considered by Patent Owner’s witness, and Dr. Koo does not grapple with how the content of those references and Patent Owner’s corresponding concessions of those challenges undermine Dr. Koo’s testimony. For example, the Petition explains how the prior art used sequence information for sequence alignment and mapping. Pet. 63-65. This uncontested argument undermines Dr. Koo’s testimony (and Patent Owner’s primary argument in this case) that the prior art operated ignorant to sequence information (nucleotide identity) and even taught away from its inclusion for downstream analysis. Dr. Koo did not consider a continuation application (same specification) or contest USPTO action issuing U.S. Pat. No. 11,844,666 (EX1045) with claims to detecting base modifications using “reaction data” from SMRT sequencing data including “basecalls.” Tsai (EX1020) was not considered by Dr. Koo but discusses “monitoring the kinetics of the sequencing reaction” for modification detection and cites the Flusberg PCT (EX1024). Pet. 69. The Petition discusses the PacBio

Template Guide as teaching “routine procedures to prepare molecules for PacBio sequencing,” but it does not identify bisulfite treatment as being required for PacBio sequencing. Pet. 65-66. Dr. Koo did not consider any of these references despite conflicts between his testimony and the objective evidence.

As another example, Dr. Koo repeats the incredible argument already rejected at the institution stage stating that PacBio’s BAM file cannot be an input data file for a model. EX2041, ¶¶128-130. But Patent Owner withheld from Dr. Koo the Wenger paper, where PacBio reports already using another deep learning model (DeepVariant) to improve variant base call accuracy in SMRT data. EX1032, Abstract, Table 1, 11 (“DeepVariant, a model trained on PacBio CCS reads”). DeepVariant takes a BAM file as input. EX1036, 1 (“takes aligned reads (in BAM or CRAM format)”).

Dr. Koo also parrots argument regarding objective indicia related 5-mC detection without bisulfite sequencing but does so without consideration of nexus between the evidence and the claimed invention. *See* EX2041, ¶¶152-165. Dr. Koo’s declaration, in fact, contains no nexus analysis or even lip service to the legal standard for nexus. *See* EX1049, 149:3-22. Dr. Koo has no such nexus analysis in his declaration because there is no nexus with the excessively broad claims. Reply 16-27. Dr. Koo’s discussion of allegedly “unexpected results” (¶¶160-166) similarly ignores pertinent evidence and the lack of nexus with the

broad scope of challenged claim 1. Claim 1 is not limited to 5-mC detection, does not exclude bisulfite treatment, and expressly encompasses, *inter alia*, a principal component analysis (PCA) model (as stated in dependent claim 11). Moreover, claim 1 has no accuracy requirement and does not exclude '794 embodiments even less accurate to what is criticized. *See, e.g.*, EX1001, Fig. 23 (AUC=0.50); Reply 19, 25. Accordingly, Dr. Koo objective indicia testimony is woefully incomplete and fails to observe the correct legal standards—his opinion in this regard should be excluded. *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010); *Meds. Co. v. Mylan Inc.*, 2014 U.S. Dist. LEXIS 38714, *15 (excluding “commercial success opinions because [the expert] failed to opine or prove that a nexus exists between the novel features of the [] patent and any alleged commercial success”).

Even where Dr. Koo identifies a reference in EX2032 or EX2055, his discussion is so factually misguided it calls into question whether Dr. Koo meaningfully considered listed references or merely parroted attorney-generated argument uncritically. For example, Dr. Koo disregards experimental examples in Flusberg-338 on the misguided basis “it doesn’t represent real data.” EX1049, 96:16-20; *see* EX2041, ¶108 (“the ’338 patent is prophetic”); *see also* EX1049, 97:18-99:11 (disregarding the experiments of Figs. 11 and 14 on the false basis they are “not experimental data,” “not realistic,” “toy,” and “cartoon”). *Contra*

EX1007, 65:46-52 (“FIG. 14 provides actual data....”).² Dr. Koo also failed to consider Flusberg-2010’s use of nucleotide identity for sequence alignment. *E.g.*, EX1006, 6 (“Reads were filtered after alignment....”), 7 (“using the standard Smith-Waterman alignment algorithm”); *see also* EX1049, 102:23-103:14. There is no dispute that sequence alignment requires nucleotide identities obtained from sequence reads. EX1049, 88:15-18. *See generally id.*, 85:9-89:16.

At ¶125 of his declaration, Dr. Koo uncritically repeats Patent Owner’s mischaracterization of Dr. Dessimoz’s deposition without realizing he is actually quoting the questioning lawyer, not Dr. Dessimoz as stated. EX1049, 146:23-148:6. Dr. Koo also mischaracterizes references like the PacBio White Paper (EX1016) based on failing to critically review their entire contents. EX1049, 117:15-118-23 (failure to consider a described “typical experiment”), 126:2-5 (admitting “[h]e’s just seen the [EX1047] document for the first time. He hasn’t

² Even if Figs. 11 and 14 of Flusberg-338 were depicting prophetic examples (they are not), it is legal error to disregard them out of hand. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1357 (Fed. Cir. 2010); *see also Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984) (rejecting the proposition that prophetic examples “do not aid one skilled in the art in making the invention”).

reviewed the entire document.”). Dr. Koo’s testimony is littered with such instances of selective review and plain error, calling into question whether he reviewed any of the documents cited in EX2032 or EX2055 either critically or entirely.

Accordingly, having failed to consider various prior art references and large swaths of the record, Dr. Koo is not able to testify as to the perspective of a POSA or offer rebuttal to a case he didn’t assess critically or entirety. Moreover, Dr. Koo’s opinions are predicated on various legal and factual errors, in addition to an incomplete analysis of the state of the art. *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) (rejecting an obviousness analysis that “narrowly focus[ed] on the four prior-art references cited by the Examiner and ignor[ed] the additional record evidence”). His declaration testimony is unhelpful, unreliable and irrelevant, and Patent owner has not demonstrated otherwise. As such, EX2041 should be excluded.

IV. EX2002 – (FIRST) PETER KOO DECLARATION

Exhibit 2002 is the declaration of Dr. Koo that was filed with Patent Owner’s Preliminary Response. EX2002 was not relied upon in Patent Owner’s post-institution briefing and is therefore irrelevant and unavailable to support Patent Owner’s rebuttal case. In addition, EX2002 suffers from the same defects discussed above with respect to Dr. Koo’s second “supplemental” declaration

(EX2041). That is, Dr. Koo failed to consider various prior art references, including many references cited and relied upon in the petition materials, and his testimony is predicated on various legal and factual errors. Dr. Koo is not able to testify as to the perspective of a POSA or offer rebuttal to a case he didn't assess critically or entirety.

To the extent EX2002 is considered, it presents unexplained inconsistencies in testimony and weighs against the credibility of Dr. Koo, including his testimony in EX2041. For example, ¶60 of EX2002 states that Tse's HK model is, at best, just one embodiment with the broad scope of claim 1. This lack of nexus between Tse and claim 1 was subsequently confirmed by Dr. Koo. *See e.g.*, Reply 16-19, 21-22. Yet, at ¶77 of EX2041, Dr. Koo states (incorrectly) that "Tse's holistic kinetic model is the model of claim 1." This is yet another illustration of Dr. Koo uncritically adopting attorney argument that is unsupported and facially inconsistent with objective evidence of record. As stated above and explained in Petitioner's Reply brief, Dr. Koo conceded the falsity of this statement both during cross-examination and elsewhere in EX2041.

Accordingly, Exhibit 2002 is irrelevant, its admission would be unduly prejudicial, misleading, and a waste of time. To the extent EX2002 is relevant, it is inconsistent with EX2041 and demonstrates the lack of credibility of Dr. Koo's testimony. The extensive volume of disregarded evidence, inconsistencies, and

errors both factual and legal should give the Board considerable pause before crediting any portion of Dr. Koo's testimony.

V. CONCLUSION

Accordingly, both EX2041 and EX2002 should be excluded.

Respectfully submitted,

Dated: January 2, 2024

/ Michael T. Rosato /
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CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing Petitioner's Motion to Exclude was served on January 2, 2025, at the following electronic service addresses:

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Respectfully submitted,

Dated: January 2, 2024

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