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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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YUK-MING DENNIS **LO**, ROSSA WAI KWUN CHIU, and KWAN CHEE  
CHAN  
Junior Party  
(Application 13/417,119),

v.

STEPHEN **QUAKE** and HEI-MUN CHRISTINA FAN  
Senior Party  
(Application 12/393,833).

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Patent Interference No. 105,924 (DK)  
(Technology Center 1600)

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**Decision on Remand**

**37 C.F.R. § 41.125**

*Before*, RICHARD E. SCHAFER, SALLY GARDNER LANE, and  
DEBORAH KATZ, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

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1 I. *Review of prior history*

2 Judgement was entered against Quake in Interference 105,924 based on the  
3 decision that the specification of the application 12/393,833 (“the ’833  
4 application”) does not provide a sufficient written description of Quake’s involved  
5 claims. (*See* Judgment, Paper 231; *see* Decision on Motion, Paper 230.)

6 As the assignee of the Quake patents and application, The Board of Trustees  
7 of the Leland Stanford Junior University appealed the judgment entered in this  
8 interference to the Court of Appeals for the Federal Circuit. (*See The Board of*  
9 *Trustees of the Leland Stanford Junior University v. The Chinese University of*  
10 *Hong Kong*, App. 2015-011 (Fed. Cir. June 27, 2017).) The Federal Circuit  
11 vacated the prior decision and remanded the case to the Board, finding error. The  
12 court’s decision refers to the issue of written description in patent 8,008,018, which  
13 is involved in Interference 105,920, but the court noted that its decision applies to  
14 the Board’s findings in the instant interference as well. (*See Board of Trustees*,  
15 slip. op. 2, n.1.) The specifications of the ’833 application and the ’018 patent are  
16 substantially the same.

17 The court determined that the Board erred by considering whether the  
18 description in the ’018 patent *precluded* targeted massively parallel sequencing,  
19 instead of considering whether the description *discloses* random massively parallel  
20 sequencing. (*See Board of Trustees*, slip op. 18.) The court also determined that  
21 the Board improperly relied on portions of Dr. Gabriel’s, Lo’s expert, testimony  
22 regarding a machine mentioned in the ’018 patent. (*See Board of Trustees*, slip op.  
23 15-18.)

24 On remand, the court instructed us to

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1 examine whether a person of ordinary skill in the art would have  
2 known, as of the priority date, that the '018 specification's reference  
3 to Illumina products meant random MPS sequencing as recited in the  
4 claims, by examining the record evidence as to pre-filing date art-  
5 related facts on Illumina products.  
6

7 (*See Board of Trustees*, slip op. 19.) We should “examine whether a person of  
8 ordinary skill would have understood that the '018 patent's specification disclosed  
9 random MPS sequencing, as opposed to whether the specification did not preclude  
10 targeted MPS sequencing.” (*See Board of Trustees*, slip op. 20.)

11 We find that even though the '833 application discusses random massively  
12 parallel sequencing and mentions identification of chromosomes from random  
13 sequence information, it does not do so in the context of Quake's claimed methods.  
14 Specifically, we find that the '833 application does not describe using the data  
15 obtained from random massively parallel sequencing and identification of  
16 chromosomes to compare the amounts of chromosomes in a mixture of maternal  
17 and fetal genomic in order to determine the presence or absence of said fetal  
18 aneuploidy, as required in step d. of Quake's claims.

19 II. *Written Description*

20 Quake's claims are directed to methods of determining whether a fetus has  
21 the wrong number of chromosomes – a condition called “fetal aneuploidy.” In the  
22 claimed methods, this determination is made by sampling a maternal tissue, for  
23 example blood, that contains both maternal and fetal DNA, instead of a sample of  
24 fetal tissue. The claimed methods are less invasive than those currently used to  
25 detect fetal aneuploidy, such as amniocentesis. (*See Board of Trustees*, slip op. at  
26 2-3.)

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1 Claim 25 of the '833 application recites:

2 A method for performing prenatal diagnosis of a fetal chromosomal  
3 aneuploidy from a plasma or serum sample of a female subject pregnant with  
4 at least one fetus, wherein the plasma or serum sample includes cell-free  
5 genomic DNA molecules from the female subject and from the at least one  
6 fetus, the method comprising:

7 *massively parallel sequencing cell-free genomic DNA molecules*  
8 *contained in the plasma or serum sample to obtain random nucleic acid*  
9 *sequences from the genomic DNA molecules of the female subject and of the*  
10 *at least one fetus;*

11 identifying at least a portion of the nucleic acid sequences as  
12 belonging to a first specific human chromosome and at least one second  
13 specific human chromosome;

14 determining a first amount of the nucleic acid sequences identified as  
15 being uniquely present on the first specific human chromosome; and

16 determining a second amount of the nucleic acid sequences identified  
17 as being uniquely present on the at least one second specific human  
18 chromosome;

19 *determining a ratio based on the first amount and the second amount,*  
20 *thereby determining a ratio of the amount of the nucleic acid sequences*  
21 *identified as being uniquely present on the first specific human chromosome*  
22 *to the amount of the nucleic acids being uniquely present on the at least one*  
23 *second specific chromosome;*

24 determining whether the ratio is statistically significant; and

25 correlating a statistically significant result with the presence of a fetal  
26 chromosomal aneuploidy on the first chromosome.

27  
28 (Quake Clean Copy of Claims, Paper 11 (emphasis added).) The other  
29 independent claims in the '833 application each include a limitation to massively  
30 parallel sequencing to obtain random nucleic acid sequences from genomic DNA  
31 of a female subject and a fetus and a limitation to determining a ratio of the amount  
32 a first specific chromosome and of a second specific chromosome identified in the  
33 sample. (*See id.*)

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1 A.

2 We address the court’s instruction to examine whether one of skill in the art  
3 would have understood that the specification of the ’833 application discloses  
4 random massively parallel sequencing. (*See Board of Trustees*, slip op. 19.) The  
5 ’833 application states, in a portion we refer to as “passage A”:

6 A methodology useful in the present invention platform is based on  
7 massively parallel sequencing of millions of fragments using  
8 attachment of randomly fragmented genomic DNA to a planar,  
9 optically transparent surface and solid phase amplification to create a  
10 high density sequencing flow cell with millions of clusters, each  
11 containing ~1,000 copies of template per sq. cm. These templates are  
12 sequenced using four-color DNA sequencing-by-synthesis  
13 technology. See, products offered by Illumina, Inc., San Diego  
14 California Also. see US 2003/0022207 to Balasubramanian, et al.,  
15 published January 30, 2003, entitled "Arrayed polynucleotides and  
16 their use in genome analysis."  
17

18 (’833 application, Exh. 1050, at ¶ 98.) Lo admits that “products offered by  
19 Illumina” were known to be products for massively parallel sequencing at the time  
20 of filing. (*See Lo Motion 1*, Paper 26, at Material Fact 49 (“[P]roducts offered by  
21 Illumina’ as mention at ’833 application includes products for [massively parallel  
22 sequencing].”); *see Quake response* (“Admitted.”).) Indeed, the passage quoted  
23 above expressly discloses massively parallel sequencing.

24 The passage also includes details of massively parallel sequencing, which  
25 the court indicated we failed to explain and compare to the claim limitations in our  
26 prior opinion. (*See Board of Trustees*, slip op. at 18-19.) Specifically, as Dr.  
27 Deter, Quake’s witness, explains, sequencing with Illumina products involves  
28 certain steps, which the ’833 application mentions by including the phrases: “using

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1 attachment of randomly fragmented genomic DNA,” “solid phase amplification,”  
2 “~1,000 copies of template,” and sequencing of templates “using four-color DNA  
3 sequencing-by-synthesis technology.” (See Detter Decl., Exh. 2049, at ¶¶ 39-40,  
4 59-70.) Lo does not dispute that these details are part of massively parallel  
5 sequencing with Illumina products. Accordingly, we find that this portion of the  
6 ’833 application expressly describes massively parallel sequencing.

7 Quake’s claims require that the massively parallel DNA sequencing be done  
8 “to obtain *random* nucleic acid sequences from the genomic DNA molecules of the  
9 female subject and of the at least one fetus . . . .” (See Quake Clean Copy of  
10 Claims, Paper 11, at 1 (emphasis added); see also *id.* at 2-6 (independent claims  
11 42, 91, 95, reciting similar language regarding random nucleic acid sequences).)  
12 Thus, as the court instructed, we consider whether the ’833 application provides a  
13 written description of sequencing randomly selected DNA fragments. (See *Board*  
14 *of Trustees*, slip op. 19.)

15 The parties agree that the claim limitation of obtaining “random nucleic acid  
16 sequences” means that the nucleic acid fragments have not been identified before  
17 the sequencing procedure and that sequence-specific primers to target specific gene  
18 loci are not required. (See Lo appl. 13/070,275, Exh. 1023, ¶ 58; see Detter Decl.  
19 Exh. 2049, at ¶ 91; see also *Board of Trustees*, at slip op. 6.) Lo also agrees that it  
20 was known that Illumina products could perform massively parallel sequencing of  
21 randomly selected DNA fragments. (See Lo Motion 1, Paper 26, at 23:17-19,  
22 Material Fact 50 (“Illumina sequencing platforms can perform either random or  
23 targeted DNA sequencing, depending on whether predetermined target DNA  
24 fragments are specifically identified or targeted prior to sequencing.”).)

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1 Passage A of the '833 application expressly states that a methodology  
2 “based on massively parallel sequencing of millions of fragments using attachment  
3 of *randomly fragmented* genomic DNA to a planar, optically transparent surface”  
4 is useful in the disclosed invention. ('833 application, Exh. 1050, at ¶ 98  
5 (emphasis added).) We agree with Lo that “randomly fragmented genomic DNA”  
6 is not necessarily the same as “DNA fragments randomly selected” from a mixture.  
7 (See Lo Reply 1, Paper 53, at 7:1-2.) But, we disagree with Lo that this passage  
8 necessarily describes target-specific analysis because targeting steps are not  
9 specifically recited in the passage. (See Lo Motion 1, Paper 26, at 9:24-10:12.)

10 Quake argues that passage A does not describe targeted sequencing and  
11 therefore must describe random sequencing. (See Quake Opp. 1, Paper 47, at 7:7-  
12 17.) Quake attempts to support its argument by citing to Material Fact 92 in  
13 Appendix 2 of its Opposition brief and to Dr. Gabriel’s testimony. (See *id.*, citing  
14 p. II-16, Material Fact 92 and Gabriel Decl., Exh. 1021, at ¶ 47.) Material Fact 92  
15 is not helpful to us. Material Fact 92 refers to a document entitled “Technology  
16 Spotlight: Illumina<sup>®</sup> Sequencing,” which is provided in Exhibit 2035, but Quake  
17 fails to show that it was publically available before the filing date of the '833  
18 application, 26 February 2009. We note that Exhibit 2035 has a copyright date of  
19 2010. (See Exhibit 2035, at 6.) We need not consider this reference because  
20 Quake has not shown that it specifically relates to “Illumina products” existing on  
21 the filing date. (See *Board of Trustees*, slip op. at 19-20.)

22 Even if we consider the content of Material Fact 92 and the document it  
23 cites, we would be unpersuaded by Quake’s argument. The summary of Exhibit  
24 2035 provided in Material Fact 92 highlights the use of non-specific primers in the

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1 Illumina platform, but this aspect is not expressly stated in the '833 application.  
2 Similarly, although Dr. Detter's testimony is cited in Material Fact 92 (*see* Detter  
3 Decl., Exh. 2049, at ¶ 146), it is virtually identical with the Material Fact and fails  
4 to explain how the express disclosure of the '833 application describes what is  
5 taught in Exhibit 2035. For example, Quake highlights the portion of the summary  
6 in Material Fact 92 that refers to using primers that are not specific for a target  
7 sequence, but this direction is not stated in the '833 application itself. Quake does  
8 not direct us to a discussion of non-specific primers or a citation to Exhibit 2035 in  
9 the '833 application. Accordingly, we do not find that Material Fact 92 supports  
10 an express description of the claimed methods.

11 Quake also argues that the Balasubramanian patent application cited in  
12 passage A "supports random massively parallel sequencing." (Quake Opp. 1,  
13 Paper 47, at 4:22-24.) The four lines of Dr. Gabriel's deposition transcript that  
14 Quake cites support Quake's argument because on cross-examination Dr. Gabriel  
15 agreed with this statement. (*See* Gabriel Depo., Exh. 2078, at 60:18-22.) Thus, we  
16 find that Balasubramanian provides some of disclosure of massively parallel  
17 sequencing of DNA fragments selected randomly.

18 In contrast, we not persuaded by Quake's argument that random massively  
19 parallel sequencing is supported by the Braslavsky article, which is disclosed  
20 elsewhere in the '833 application. (Quake Opp. 1, Paper 47, at 4:24-5:1; *see* '833  
21 appl., Exh. 1050, at ¶¶ 10 and 96.) According to Quake, Dr. Gabriel's testimony  
22 supports this argument because the Braslavsky article was "the concept behind the  
23 Helicos sequencer, which could be used for random sequencing." (Quake Opp. 1,  
24 Paper 47, at 4:25-26, citing Gabriel Depo., Exh. 2078, at 92:6-94:2.) Because

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1 Quake does not direct us to discussion of the Helicos sequencer in the '833  
2 application, we are not persuaded by this argument. (*See Board of Trustees*, slip  
3 op. at 17 (“All of the published references on which the Board relies focus on the  
4 Roche 454 platform, not the Illumina platform actually referenced in the  
5 specification.”))

6 Accordingly, we find that passage A of the '833 application expressly  
7 describes massively parallel sequencing. The only portion, though, of passage A  
8 that ties this sequencing to the random sequence information mentioned in passage  
9 B is the citation to Balusubramanian, as characterized by four lines of Dr. Gabriel's  
10 testimony.

11 B.

12 Immediately following passage A, the '833 application also states, in a  
13 portion we refer to as “passage B”:

14  
15 Sequencing may be combined with amplification-based methods in a  
16 microfluidic chip having reaction chambers for both PCR and  
17 microscopic template-based sequencing. Only about 30 bp of random  
18 sequence information are needed to identify a sequence as belonging  
19 to a specific human chromosome. Longer sequences can uniquely  
20 identify more particular targets. An algorithm for designing unique  
21 sequences is described in Yamada. et al. [Exhibit 1016] illustrative of  
22 software methods that can be used to identify a sequence in  
23 comparison to the known genome sequence. See, also Zhu et al.,  
24 [Exhibit 1017] describing a single-molecule-based technology for  
25 studying mRNA.

26  
27 ('833 application, at ¶ 99.) Lo argues that, based on the citations to Yamada and  
28 Zhu, passage B refers to designing primers for the targeted digital PCR analysis

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1 described in the rest of the '833 application, not to random massively parallel  
2 sequencing. (*See* Lo Motion 1, Paper 26, at 11:28-12:17.) Quake opposes Lo's  
3 argument by arguing that this passage refers to alignment of the sequence reads  
4 produced from random sequencing. (Quake Opp. 1, Paper 47, at 9:21-10:8.)

5 Passage B expressly recites "random sequence information." Accordingly,  
6 even if the Yamada and Zhu references that follow are not relevant to random  
7 sequence information, we find that passage B does expressly describe random  
8 sequencing.

9 C.

10 We find that passage A and passage B of the '833 application provide some  
11 express description of individual elements recited in Quake's claims. "Massively  
12 parallel sequencing" is expressly described, as is random sequencing. These  
13 activities are linked in the Balasubramanian reference.

14 Our task is to determine whether these disclosures are sufficient to have  
15 demonstrated one of ordinary skill in the art that the inventors were in possession  
16 of a method of determining fetal aneuploidy with random massively parallel  
17 sequencing as claimed by Quake. Although the express language describes some  
18 of the elements of the claimed method, we find that it is not sufficient to provide a  
19 written description under 35 U.S.C. § 112, first paragraph, because the '833  
20 application does not tie these elements together into a complete method and does  
21 not explain how to use the data from random massively parallel sequencing of a  
22 mixture of genomic DNA to determine fetal aneuploidy.

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1 D.

2 The insufficiency of the description of random massively parallel  
3 sequencing in the '833 application is apparent when it is compared to the  
4 description of a different method, called digital analysis, in that patent. The parties  
5 agree that the '833 application sufficiently describes the digital analysis method of  
6 determining fetal aneuploidy from a mixed sample. (*See* Lo Motion 1, Paper 26, at  
7 20:1-2, Material Fact 11 (“The '833 Application discloses ‘digital analysis’ method  
8 for detecting fetal aneuploidy.”) and Quake Opp. 1, Paper 47, at II-3 (admitting Lo  
9 Material Fact 11).) Specifically, the '833 application recites, in part:

10 Thus, the present method [of digital analysis] comprises generally the  
11 following steps:

- 12 1. Obtaining a tissue containing DNA from a pregnant subject, . . . .
- 13 2. Distributing single DNA molecules from this sample to a number of  
14 discrete reaction samples, where the number of reaction samples is  
15 selected to give a statistically significant result for the number of  
16 copies of a target in the DNA molecules. . . .
- 17 3. Detecting the presence of the target in the DNA in a large number  
18 of reaction samples, preferably with a sequence specific technique  
19 such as highly multiplexed short read sequencing or a PCR  
20 reaction wherein the PCR product is labeled to give a convenient  
21 quantitative read out . . . . and
- 22 4. Quantitative analysis of the detection of the maternal and fetal  
23 target sequences.

24  
25 ('833 appl., Exh. 1050, at ¶ 41.) Thus, the '833 application outlines the specific  
26 steps one would take to perform digital analysis with a sequence specific technique  
27 such as sequencing or a PCR reaction.

28 In contrast, the disclosures in the '833 application that relate to a method of  
29 random massively parallel sequencing are the mention of massively parallel

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1 sequencing of randomly fragmented DNA, “products offered by Illumina,” citation  
2 to Balasubramanian, and a sentence about the number of base pairs needed to  
3 identify the chromosomal origin of a sequence. The ’833 application does not  
4 recite specific series of steps one would take to determine whether fetal aneuploidy  
5 exists using random massively parallel sequencing.

6 We find that the ’833 application fails to provide *express* “blazemarks” of a  
7 method of massively parallel sequencing of DNA fragments randomly selected  
8 from a mixture to determine fetal aneuploidy. *See In re Ruschig*, 379 F.2d 990,  
9 994–95 (C.C.P.A. 1967) (analogizing, where the disclosure recited a list of  
10 possible reactants, but failed to highlight the necessary one, that “[i]t is an old  
11 custom in the woods to mark trails by making blaze marks on the trees. It is no  
12 help in finding a trail or in finding one's way through the woods where the trails  
13 have disappeared— or have not yet been made, which is more like the case here—  
14 to be confronted simply by a large number of unmarked trees.”)

15 E.

16 In the absence of an *express* written description, the ’833 application could  
17 still provide a sufficient description of the claimed methods if one of ordinary skill  
18 in the art would have understood from what was expressly described that the  
19 inventors were in possession of the inventions. *See Fujikawa v. Wattanasin*, 93  
20 F.3d 1559, 1570 (Fed. Cir. 1996) (“As the Board recognized, however, *ipsis verbis*  
21 disclosure is not necessary to satisfy the written description requirement of section  
22 112. Instead, the disclosure need only reasonably convey to persons skilled in the  
23 art that the inventor had possession of the subject matter in question.”). Thus, we  
24 look to how one of ordinary skill in the art would have understood the claims as a

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1 whole. We find that the '833 application does not describe how to analyze the data  
2 that would be obtained from massively parallel sequencing to determine if fetal  
3 aneuploidy is present and that, thus, one of ordinary skill in the art would not know  
4 that the inventors possessed a method of determining fetal aneuploidy.

5 Quake's claims require that after determining the amounts of nucleic acid  
6 sequences for a first and a second human chromosome, "a ratio based on the first  
7 amount and the second amount" is determined and used to correlate with or  
8 identify fetal aneuploidy. (Quake Clean Copy of Claims, Paper 11.) Lo argues  
9 that because the '833 application focuses on detecting aneuploidy based on a 1:1  
10 ratio between predetermined sequences from two chromosomes, which is  
11 appropriate for digital analysis (*see* '833 appl., Exh. 1050, at ¶¶104-106), it does  
12 not describe the considerations that must be made when comparing data from  
13 massively parallel sequencing of DNA fragments randomly selected. (Lo Motion  
14 1, Paper 26, at 17:1-18:21, citing Gabriel Decl., Exh. 1049, at ¶¶ 109-110; *see also*  
15 Lo Reply 1, Paper 53, at 8:23-9:5.)

16 Lo bases its argument on Dr. Gabriel's testimony that because human  
17 chromosomes are not all the same size, randomly selected fragments are more  
18 likely to be identified from larger chromosomes than from smaller chromosomes.  
19 (Gabriel Decl., Exh. 1049, at ¶ 109.) According to Dr. Gabriel, given an equal  
20 number of all chromosomes, there is a greater chance that a random fragment will  
21 be from a larger chromosome than a smaller one. A method relying on random  
22 massively parallel sequencing cannot rely on a 1:1 ratio of sequences because even  
23 in the absence of aneuploidy, the number of random sequence reads aligning to a  
24 larger chromosome versus those aligning to a smaller chromosome will always

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1 result in a ratio greater than 1:1. (Gabriel Decl., Exh. 1049, at ¶ 109.) Dr. Gabriel  
2 explains that instead of focusing on deviations from a 1:1 ratio, methods that use  
3 massively parallel sequencing of randomly selected fragments must take into  
4 consideration the size of the chromosomes before determining a ratio that  
5 represents a normal number of chromosomes. (See Gabriel Decl., Exh. 1049, at ¶  
6 110.)

7 Quake does not dispute that a random massively parallel sequencing method  
8 for determining fetal aneuploidy would need to take into account the length of the  
9 chromosomes being analyzed and could not be based on deviations from a 1:1  
10 ratio. Instead, Quake argues that Dr. Gabriel admitted that statistical tests  
11 reportedly disclosed in the '833 application could be used to determine aneuploidy.  
12 (Quake Opp. 1, Paper 47, at 10:10-24, citing Gabriel Depo., Exh. 2078, at 51:2-  
13 53:16 and 73:22-74:18; see Detter Decl., Exh. 2082, at ¶ 29.) We do not find that  
14 the cited cross-examination refers to disclosures in the '833 application  
15 specification. Instead, Dr. Gabriel testifies about statistical methods, such as the  
16 “T-test” and the “Z-test,” and how they could be used in general. (See Gabriel  
17 Depo., Exh. 2078, at 51:2-53:16 and 73:22-74:18.) Quake also argues that Dr.  
18 Gabriel testified that the fraction of a sample comprising a given chromosome is  
19 consistent from individual to individual in the absence of aneuploidy. (See Quake  
20 Opp. 1, Paper 47, at 10:17-19, citing Gabriel Depo, Exh. 2078, at 54:1-56:2.) We  
21 do not find that the testimony Quake cites addresses the statistical analysis needed  
22 when using sequences from chromosomes of differing lengths. None of the  
23 testimony is evidence that Dr. Gabriel admitted statistical methods relying on the

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1 different lengths of identified chromosomes were described in the '833 application  
2 specification.

3 Quake also argues that the evidence Lo submitted with its Priority Statement  
4 (*see* Paper 24; Ex. 2074) and Lo's provisional application (Exh. 2010) contain less  
5 disclosure than the Quake '833 application about the statistical analysis used to  
6 assess fetal aneuploidy. (Quake Opp. 1, Paper 47, at 4:3-11, citing Gabriel Depo.,  
7 Exh. 2078, at 33:11-34:4 and 38:5-12.) Presumably Quake's argument is that a  
8 description of the statistical analysis is not necessary because it not present in Lo's  
9 other documents. This argument is not persuasive because written description  
10 support is evaluated on what is described in specification at issue. Whether or not  
11 Lo's other documents provide sufficient written description is not at issue.

12 Quake argues further that Dr. Detter explained how the '833 application  
13 discloses a method that "intrinsically corrects for biases due to chromosome size  
14 by comparing results from a test sample to normal samples using statistical  
15 methods, such as a Student's T-test." (*See* Quake Opp. 1, Paper 47, at 3:4-19),  
16 citing Detter Decl., Exh. 2082, at ¶¶ 13 and 29, and '018 patent, Exh. 1022, at  
17 5:64-6:3 and 28:5-34 (which correspond to '833 appl., Exh. 1050, at ¶¶ 27 and  
18 148, Table 1.) This argument is not supported by the cited portions of the '833  
19 application. Paragraphs 13 and 29 of Dr. Detter's declaration address Dr. Gabriel's  
20 cross-examination testimony about what was known in the art of normalized  
21 frequencies, chromosome size, and generalized statistical analyses. (*See* Lo Reply,  
22 Paper 53, at 9:11-19.) This testimony does not explain anything about the  
23 specification of the '833 application. Similarly, the portions of the '833  
24 application that Quake cites do not mention chromosome size and do not discuss

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1 any “intrinsic correction.” The portions refer only to statistical significance in  
2 general (*see* ’833 appl., Exh. 1050, at ¶ 27) and to analysis based on a 1:1 ratio (*see*  
3 *id.* at ¶ 148, Table 1).

4 Quake argues further that those of skill in the art would have known how to  
5 correct for chromosome size in February 2007, relying on Dr. Gabriel’s testimony.  
6 (*See* Quake Opp. 1, Paper 47, at 3:14-18; citing Detter Decl., Exh. 2082, at ¶ 13,  
7 and Gabriel Depo., Exh. 2078, at 34:13-35:9.) In the portion of her testimony cited  
8 by Quake, Dr. Gabriel testifies that it was well known at the time how to create a  
9 “normalized frequency,” but her testimony is about the disclosure of Lo’s priority  
10 statement (Exhibit 2074), not the ’018 patent. (*See* Gabriel Depo., Exh. 2078, at  
11 34:13-35:9.) Specifically, Dr. Gabriel addresses Example 3 of Exhibit 2074, which  
12 provides for random sequencing and states:

13 By taking into account of the relative size of chromosome 21  
14 compared with the other chromosome, one could obtain a normalized  
15 frequency, within a reference range, of chromosome 21-specific  
16 sequences from such a sequencing exercise. If the fetus has trisomy  
17 21, then the normalized frequency of chromosome 21-derived  
18 sequences from such a sequencing exercise will increase, thus allow  
19 the detection of trisomy 21.

20  
21 (Exh. 2074, at 11, *see* Gabriel Depo., Exh. 2078, at 34:17-19 (referring to Example  
22 3 of Exh. 2074 “It actually says you've got to take into account the chromosome  
23 size of things you're comparing.”).) Quake does not direct us to similar discussion  
24 of “normalized frequency” in the ’833 application.

25 Quake’s argument is that those of skill in the art would have known *how* to  
26 normalize the frequency of sequence reads by the size of the chromosome, but  
27 Quake does not direct us to a portion of the ’833 application that describes the need

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1 to do so. Accordingly, we are persuaded that one of ordinary skill in the art would  
2 not have considered that the inventors of the '833 application contemplated a  
3 method requiring this statistical analysis.

4 The '833 application specification does not provide a description of an  
5 analysis that compares the amounts of the identified chromosomes determined  
6 from random massively parallel sequencing data and determines the presence or  
7 absence of fetal aneuploidy. In the absence of a description of such analysis, we  
8 are persuaded that the express teachings in the specification about equipment  
9 useful for random massively parallel sequencing and techniques for determining  
10 sequences are not sufficient to demonstrate possession of the claimed method for  
11 “determining presence or absence of fetal aneuploidy in a maternal tissue sample  
12 comprising fetal and maternal genomic DNA.” Instead, the description in the '833  
13 application indicates that the inventors had only “a mere wish or plan” to use this  
14 new technology in their invention. *Centocor Ortho Biotech, Inc. v. Abbott Labs.*,  
15 636 F.3d 1341, 1351 (Fed. Cir. 2011); *Regents of the Univ. of Cal. v. Eli Lilly &*  
16 *Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997).

17 In light of the Federal Circuit’s remand, we are persuaded that the '833  
18 application fails to describe the methods claimed by Quake as required under 35  
19 U.S.C. § 112. Accordingly, we grant Lo Motion 1.

### 20 III. Conclusion

21 During prosecution of the '833 application, Quake stated numerous times  
22 that the pending claims were amended and new claims were added to “track” the  
23 amendments and new claims made in Lo application 12/178,181 (“the '181  
24 application”). The '181 application is not involved in this interference, but is

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1 involved in related interference 105,923, in which Quake's '833 application is also  
2 involved. Lo's '181 application was published on 29 January 2009, as U.S. Patent  
3 Application Publication 2009/0029377, before Quake's '833 application was filed  
4 on 26 February 2009. Quake stated that it filed and amended the claims of the  
5 '833 application to anticipate or render obvious Lo's '181 application claims. (*See*  
6 *Amendment in the '833 appl., filed 6 June 2011 at 12-13; see also Amendments in*  
7 *the '833 appl., filed 29 January 2010, 12 October 2011, 27 January 2012.*)

8       Because Quake's involved application does not provide a sufficient written  
9 description to support the claims that "tracked" Lo's claims, Quake's claims are  
10 unpatentable to Quake and Quake should not have been able to challenge Lo's  
11 claims with them. We make this determination even though Lo's application  
12 involved in this interference was published on 16 August 2012, after Quake's  
13 claims were filed on 26 February 2009, because Quake's claims are directed to the  
14 same subject matter as Lo's claims involved in the 105,923 interference.<sup>1</sup>  
15 Accordingly, Quake does not have standing in this proceeding and we determine  
16 that the written description of Quake's claims to be a threshold issue. . (*See* 37  
17 C.F.R. § 41.201 (defining "threshold issue" as one which, if resolved in favor of  
18 the movant, would deprive the opponent of standing in the interference, for  
19 example, unpatentability for lack of written description under 35 U.S.C. § 112 of  
20 an involved application where the applicant's claims were first made after the  
21 publication of a movant's application and the applicant could have suggested an  
22 interference).)

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<sup>1</sup> The counts in both this interference and the '105,923 interference include Quake '833 application claim 25, as well as Lo claims involved in each interference.

Interference 105,924

1           Accordingly, we need not decide Quake Motion 1 (Paper 43) or Lo Motion 5  
2 (Paper 27). We enter judgment, in a separate paper, against Quake.

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cc (via electronic delivery):

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**CERTIFICATE OF FILING**

The undersigned hereby certifies that the original version of the foregoing **QUAKE NOTICE OF APPEAL** was filed by hand on this 30<sup>th</sup> day of March 2018, with the Director of the United States Patent and Trademark Office, at the following address:

Director of the United States Patent and Trademark Office  
c/o Office of the General Counsel  
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**CERTIFICATE OF FILING**

The undersigned hereby certifies that a true and correct copy of the foregoing **QUAKE NOTICE OF APPEAL** was filed electronically on this 30<sup>th</sup> day of March 2018, with the Patent Trial and Appeal Board, using the Interference Web Portal.

**CERTIFICATE OF FILING**

The undersigned hereby certifies that a true and correct copy of the foregoing **QUAKE NOTICE OF APPEAL** (including the filing fee) was filed electronically on this 30<sup>th</sup> day of March 2018, with the Clerk's Office of the United States Court of Appeals for the Federal Circuit, using the Court's CM/ECF filing system.

**CERTIFICATE OF SERVICE**

The undersigned hereby certifies that a true and correct copy of the foregoing **QUAKE NOTICE OF APPEAL** was served by electronic mail on this 30<sup>th</sup> day of March 2018, on all counsel of record for Junior Party Lo. In addition, on this 30<sup>th</sup> day of March 2018, a true and

correct copy of the foregoing **QUAKE NOTICE OF APPEAL** was served by overnight courier  
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Respectfully Submitted,

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