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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

STEPHEN **QUAKE** and HEI-MUN CHRISTINA FAN
Junior Party
(Patent 8,008,018),

v.

YUK-MING DENNIS **LO**, ROSSA WAI KWUN CHIU,
and KWAN CHEE CHAN
Senior Party

(Application 13/070,275).

Patent Interference No. 105,920 (DK)
(Technology Center 1600)

Judgment

37 C.F.R. § 41.127

Before, SALLY GARDNER LANE, JAMES T. MOORE, and
DEBORAH KATZ, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

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Following the Decision on Remand (“Decision,” Paper 273), Quake was ordered to show why the interference should continue to a priority or derivation phase. (*See* “Order,” Paper 274.) The Order was issued because Quake asserted dates of conception and derivation in its Priority Statement earlier than the dates accorded to and asserted by Lo. (Compare Quake Priority Statement, Paper 57, with Redeclaration, Paper 43, and Lo Priority Statement, Paper 52.) Quake failed, though, to “[p]rovide a copy of the earliest document upon which [Quake] will rely to show conception” with its Priority Statement as required under 37 C.F.R. § 41.204(2)(iv). Instead, Quake asserted that “the earliest document proving conception is a communication between Dr. Stephen Quake and his attorney dated January 2, 2006, that is subject to attorney client privilege.” (Quake Priority Statement, Paper 57, at 2:25-3:1.) The Order to Show Cause provided Quake an opportunity to submit this document.

In its Response to the Order to Show Cause, Quake did not submit a copy of the communication between Dr. Quake and his attorney. Instead, Quake submitted a copy of Quake’s application 11/701,686 (“the ’686 application”), filed on February 2, 2007 (Exh. 2004¹) as the earliest document on which it intends to rely. (Response to Order to Show Cause (“Response”), Paper 275, at 3:8–9.)

In the Decision on Remand, the Board determined that the ’686 application is not a constructive reduction to practice of the Count in this Interference. (*See* Decision, Paper 273, at 17:11–21:5.) We denied Quake’s request for rehearing of

¹ We note that Quake cites Exhibit 2002, while Quake Exhibit List (Paper 265) identifies the ’686 application as Exhibit 2004.

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that Decision. (Decision on Request for Rehearing, Paper 277.) The arguments Quake puts forth in its response to the Order to Show Cause are similar to those it raised in its Request for Rehearing. For example, Quake argues that there is testimony in the record showing that methods were well-known at the time the '686 application was filed to utilize sequence/statistical analyses on individually sequenced samples, and that those methods would have been equally applicable to the sequence data obtained in Quake's sequenced mixed sample. (*See* Response, Paper 275, at 4:20–25.) Quake argues that methods were well known in the prior art that could be applied to carry out the method of the Count, along with the disclosures of the '686 application. (*See* Response, Paper 275, at 5:11-13.)

As discussed in the Decision on Request for Rehearing, Quake's arguments do not persuade us that the decision to deny Quake benefit of its '686 application should be modified. (*See* Decision on Request for Rehearing, Paper 277.) Because we determine that the '686 application is not a reduction to practice of the Count, Quake has failed to show why it will prevail over Lo in a priority or derivation phase. Quake does not submit any other evidence of an earlier conception, reduction to practice, or derivation.

Quake also argues that the interference should proceed to a priority phase because of the determination in Interference 105,922 that Quake had an actual reduction to practice of the sequencing embodiment of the Count prior to the filing date accorded to Lo in that proceeding. (Response, Paper 275, at 5:16–19.) The count of Interference 105,922 was different from the current count and the specifications of Quake's currently involved patent and applications are different from the Quake specifications involved in that interference. Accordingly, the

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determination of priority in that interference is not dispositive of the issues of this interference.

Because Quake has failed to submit a document on which it can rely to show priority earlier than Lo's accorded priority date and has failed to provide a persuasive reason why this interference should continue to a priority or derivation phase, we enter judgment against Quake as to Count 1, the sole count in the interference.

It is ORDERED that claims 1-4 of Quake's involved patent 8,008,018 be CANCELED 35 U.S.C. § 135(a);

FURTHER ORDERED that a copy of this judgment be entered in the administrative records of the involved 8,008,018 patent and 13/070,275 application.

FURTHER ORDERED that a party seeking judicial review timely serve notice on the Director of the United States Patent and Trademark Office. 37 C.F.R. §§ 90.1 and 104.

FURTHER ORDERED that the parties are directed to 35 U.S.C. § 135(c) and to 37 C.F.R. § 41.205 regarding the filing of settlement agreements.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

STEPHEN **QUAKE** and HEI-MUN CHRISTINA FAN
Junior Party
(Patent 8,008,018),

v.

YUK-MING DENNIS **LO**, ROSSA WAI KWUN CHIU,
and KWAN CHEE CHAN
Senior Party

(Application 13/070,275).

Patent Interference No. 105,920 (DK)
(Technology Center 1600)

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 Interferences 105,920 based on the
3 decision that the specifications of the 8,008,018 patent (“the ’018 patent”) does not
4 provide a sufficient written description of Quake’s involved claims. (*See*
5 Judgment, Paper 259; *see* Decision on Motion, Paper 258.)

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.

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

19 On remand, the court instructed us to

20 examine whether a person of ordinary skill in the art would have
21 known, as of the priority date, that the ’018 specification’s reference
22 to Illumina products meant random MPS sequencing as recited in the
23 claims, by examining the record evidence as to pre-filing date art-
24 related facts on Illumina products.
25

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

5 We find that even though the ’018 patent discusses random massively
6 parallel sequencing and mentions identification of chromosomes from random
7 sequence information, it does not do so in the context of Quake’s claimed methods.
8 Specifically, we find that the ’018 patent does not describe using the data obtained
9 from random massively parallel sequencing and identification of chromosomes to
10 compare the amounts of chromosomes in a mixture of maternal and fetal genomic
11 in order to determine the presence or absence of said fetal aneuploidy, as required
12 in step d. of Quake’s claims.

13 II. *Written Description in the ’018 patent*

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

21 Quake claim 1, the only independent claim in the ’018 patent, recites:

22 A method for determining presence or absence of fetal
23 aneuploidy in a maternal tissue sample comprising fetal and maternal
24 genomic DNA, wherein the method comprises:

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- 1 a. obtaining a mixture of fetal and maternal genomic DNA from
- 2 said maternal tissue sample;
- 3 b. *conducting massively parallel DNA sequencing of DNA*
- 4 *fragments randomly selected from the mixture of fetal and maternal*
- 5 *genomic DNA of step a) to determine the sequence of said DNA*
- 6 *fragments;*
- 7 c. identifying chromosomes to which the sequences obtained in
- 8 step b) belong;
- 9 d. *using the data of step c) to compare an amount of at least*
- 10 *one first chromosome in said mixture of maternal and fetal genomic*
- 11 *DNA to an amount of at least one second chromosome in said mixture*
- 12 *of maternal and fetal genomic DNA, wherein said at least one first*
- 13 *chromosome is presumed to be euploid in the fetus, wherein said at*
- 14 *least one second chromosome is suspected to be aneuploid in the*
- 15 *fetus, thereby determining the presence or absence of said fetal*
- 16 *aneuploidy.*

17
18 (Quake Clean Copy of Claims, Paper 7 (emphasis added).)

19 A.

20 We address the court's instruction to examine whether one of skill in the art
21 would have understood that the '018 patent discloses random massively parallel
22 sequencing. (*See Board of Trustees*, slip op. 19.) The '018 patent states, in a
23 portion we refer to as "passage A":

24 A methodology useful in the present invention platform is based on
25 massively parallel sequencing of millions of fragments using
26 attachment of randomly fragmented genomic DNA to a planar,
27 optically transparent surface and solid phase amplification to create a
28 high density sequencing flow cell with millions of clusters, each
29 containing ~1,000 copies of template per sq. cm. These templates are
30 sequenced using four-color DNA sequencing-by-synthesis
31 technology. See, products offered by Illumina, Inc., San Diego Calif.
32 Also. see US 2003/0022207 to Balasubramanian, et al.. published Jan.

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1 30. 2003, entitled "Arrayed polynucleotides and their use in genome
2 analysis."
3

4 ('018 patent, Exh. 1022, at 19:59-20:3.) The parties agree that “products offered
5 by Illumina” were known to be products for massively parallel sequencing at the
6 time of filing. (See Lo Motion 1, Paper 54, at Material Fact 44 (“[P]roducts
7 offered by Illumina’ as mention at ’018 patent 19:67 includes products for
8 [massively parallel sequencing].”); see Quake response (“Admitted.”).) Indeed, the
9 passage quoted above expressly discloses massively parallel sequencing.

10 The passage also includes details of massively parallel sequencing, which
11 the court indicated we failed to explain and compare to the claim limitations in our
12 prior opinion. (See *Board of Trustees*, slip op. at 18-19.) Specifically, as Dr.
13 Detter, Quake’s witness, explains, sequencing with Illumina products involves
14 certain steps, which the ’018 patent mentions by including the phrases: “using
15 attachment of randomly fragmented genomic DNA,” “solid phase amplification,”
16 “~1,000 copies of template,” and sequencing of templates “using four-color DNA
17 sequencing-by-synthesis technology.” (See Detter Decl., Exh. 2049, at ¶¶ 39-40,
18 59-70.) Lo does not dispute that these details are part of massively parallel
19 sequencing with Illumina products. Accordingly, we find that this portion of the
20 ’018 patent expressly describes massively parallel sequencing.

21 Quake’s claims require that the massively parallel DNA sequencing be done
22 on “DNA fragments *randomly* selected from the mixture of fetal and maternal
23 genomic DNA” (See Quake Clean Copy of Claims, Paper 7, at A-1 (emphasis
24 added).) Thus, as the court instructed, we consider whether the ’018 patent

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1 provides a written description of sequencing randomly selected DNA fragments.

2 (*See Board of Trustees*, slip op. 19.)

3 The parties agree that the claim limitation of sequencing “DNA fragments
4 randomly selected from the mixture of fetal and maternal genomic DNA” means
5 that the nucleic acid fragments sequenced have not been identified before the
6 sequencing procedure and that sequence-specific primers to target specific gene
7 loci are not required. (*See* ’275 appl., Exh. 1023, ¶ 58; *see* Detter Decl. Exh. 2049,
8 at ¶ 91; *see also Board of Trustees*, at slip op. 6.) Lo also agrees that it was known
9 that Illumina products could perform massively parallel sequencing of randomly
10 selected DNA fragments. (*See* Lo Motion 1, Paper 54, at 23:5-7, Material Fact 45
11 (“Illumina sequencing platforms can perform either random or targeted DNA
12 sequencing, depending on whether predetermined target DNA fragments are
13 specifically identified or targeted prior to sequencing.”).)

14 Passage A of the ’018 patent expressly states that a methodology “based on
15 massively parallel sequencing of millions of fragments using attachment of
16 *randomly fragmented* genomic DNA to a planar, optically transparent surface” is
17 useful in the disclosed invention. (’018 patent, Exh. 1022, at 19:59-62 (emphasis
18 added).) We agree with Lo that “randomly fragmented genomic DNA” is not
19 necessarily the same as “DNA fragments randomly selected” from a mixture. (*See*
20 Lo Reply 1, Paper 79, at 7:4-6.) But, we disagree with Lo that this passage
21 necessarily describes target-specific analysis because targeting steps are not
22 specifically recited in the passage. (*See* Lo Motion 1, Paper 54, at 10:9-25.)

23 Quake argues that passage A does not describe targeted sequencing and
24 therefore must describe random sequencing. (*See* Quake Opp. 1, Paper 73, at 7:5-

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1 14.) Quake attempts to support its argument by citing to Material Fact 87 in
2 Appendix 2 of its Opposition brief and to Dr. Gabriel's testimony. (*See id.*, citing
3 p. II-15, Material Fact 87 and Gabriel Decl., Exh. 1021, at ¶ 47.) Material Fact 87
4 is not helpful to us. Material Fact 87 refers to a document entitled "Technology
5 Spotlight: Illumina® Sequencing," which is provided in Exhibit 2035, but Quake
6 fails to show that it was publically available before the filing date of the application
7 that became the '018 patent, 26 February 2009. We note that Exhibit 2035 has a
8 copyright date of 2010. (*See* Exhibit 2035, at 6.) We need not consider this
9 reference because Quake has not shown that it specifically relates to "Illumina
10 products" existing on the filing date. (*See Board of Trustees*, slip op. at 19-20.)

11 Even if we consider the content of Material Fact 87 and the document it
12 cites, we would be unpersuaded by Quake's argument. The summary of Exhibit
13 2035 provided in Material Fact 87 highlights the use of non-specific primers in the
14 Illumina platform, but this aspect is not expressly stated in the '018 patent.
15 Similarly, although Dr. Detter's testimony is cited in Material Fact 87 (*see* Detter
16 Decl., Exh. 2049, at ¶ 146), it is virtually identical with the Material Fact and fails
17 to explain how the express disclosure of the '018 patent describes what is taught in
18 Exhibit 2035. For example, Quake highlights the portion of the summary in
19 Material Fact 87 that refers to using primers that are not specific for a target
20 sequence, but this direction is not stated in the '018 patent itself. Quake does not
21 direct us to a discussion of non-specific primers or a citation to Exhibit 2035 in the
22 '018 patent. Accordingly, we do not find that Material Fact 87 supports an
23 express description of the claimed methods.

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1 Quake also argues that the Balasubramanian patent application cited in
2 passage A “supports random massively parallel sequencing.” (Quake Opp. 1,
3 Paper 73, at 4:20-23.) The four lines of Dr. Gabriel’s deposition transcript that
4 Quake cites support Quake’s argument because on cross-examination Dr. Gabriel
5 agreed with this statement. (*See* Gabriel Depo., Exh. 2078, at 60:18-22.) Thus, we
6 find that Balasubramanian provides some of disclosure of massively parallel
7 sequencing of DNA fragments selected randomly.

8 In contrast, we not persuaded by Quake’s argument that random massively
9 parallel sequencing is supported by the Braslavsky article, which is disclosed
10 elsewhere in the ’018 patent. (Quake Opp. 1, Paper 73, at 4:23-27; *see* ’018 patent,
11 Exh. 1022, at 2:23-29 and 19:14-22.) According to Quake, Dr. Gabriel’s testimony
12 supports this argument because the Braslavsky article was “the concept behind the
13 Helicos sequencer, which could be used for random sequencing.” (Quake Opp. 1,
14 Paper 73, at 4:24-25, citing Gabriel Depo., Exh. 2078, at 92:6-94:2.) Because
15 Quake does not direct us to discussion of the Helicos sequencer in the ’018 patent,
16 we are not persuaded by this argument. (*See Board of Trustees*, slip op. at 17 (“All
17 of the published references on which the Board relies focus on the Roche 454
18 platform, not the Illumina platform actually referenced in the specification.”))

19 Accordingly, we find that passage A of the ’018 patent expressly describes
20 massively parallel sequencing. The only portion, though, of passage A that ties
21 this sequencing to the random sequence information mentioned in passage B is the
22 citation to Balusubramanian, as characterized by four lines of Dr. Gabriel’s
23 testimony.

24

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1 B.

2 Immediately following passage A, the '018 patent also states, in a portion we
3 refer to as “passage B”:

4
5 Sequencing may be combined with amplification-based methods in a
6 microfluidic chip having reaction chambers for both PCR and
7 microscopic template-based sequencing. Only about 30 bp of random
8 sequence information are needed to identify a sequence as belonging
9 to a specific human chromosome. Longer sequences can uniquely
10 identify more particular targets. An algorithm for designing unique
11 sequences is described in Yamada. et al. [Exhibit 1016] illustrative of
12 software methods that can be used to identify a sequence in
13 comparison to the known genome sequence. See, also Zhu et al.,
14 [Exhibit 1017] describing a single-molecule-based technology for
15 studying mRNA.

16
17 ('018 patent, Exh. 1022, at 20:4-20.) Lo argues that, based on the citations to
18 Yamada and Zhu, passage B refers to designing primers for the targeted digital
19 PCR analysis described in the rest of the '018 patent, not to random massively
20 parallel sequencing. (*See* Lo Motion 1, Paper 54, at 12:6-13:5.) Quake opposes
21 Lo's argument by arguing that this passage refers to alignment of the sequence
22 reads produced from random sequencing. (Quake Opp. 1, Paper 73, at 9:24-
23 10:10.)

24 Passage B expressly recites “random sequence information.” Accordingly,
25 even if the Yamada and Zhu references that follow are not relevant to random
26 sequence information, we find that passage B does expressly describe random
27 sequencing.

28 C.

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1 We find that passage A and passage B of the '018 patent provide some
2 express description of individual elements recited in Quake's claims. "Massively
3 parallel sequencing" is expressly described, as is random sequencing. These
4 activities are linked in the Balasubramanian reference.

5 Our task is to determine whether these disclosures are sufficient to have
6 demonstrated one of ordinary skill in the art that the inventors were in possession
7 of a method of determining fetal aneuploidy with random massively parallel
8 sequencing as claimed by Quake. Although the express language describes some
9 of the elements of the claimed method, we find that it is not sufficient to provide a
10 written description under 35 U.S.C. § 112, first paragraph, because the '018 patent
11 does not tie these elements together into a complete method and does not explain
12 how to use the data from random massively parallel sequencing of a mixture of
13 genomic DNA to determine fetal aneuploidy.

14 D.

15 The insufficiency of the description of random massively parallel
16 sequencing in the '018 patent is apparent when it is compared to the description of
17 a different method, called digital analysis, in that patent. The parties agree that the
18 '018 patent sufficiently describes the digital analysis method of determining fetal
19 aneuploidy from a mixed sample. (*See* Lo Motion 1, Paper 54, at 19:16-17,
20 Material Fact 7 ("The '018 Patent discloses 'digital analysis' method for detecting
21 fetal aneuploidy.") and Quake Opp. 1, Paper 73, at II-2 (admitting Lo Material Fact
22 7).) Specifically, the '018 patent recites, in part:

23 Thus, the present method [of digital analysis] comprises generally the
24 following steps:

25 1. Obtaining a tissue containing DNA from a pregnant subject,

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- 1 2. Distributing single DNA molecules from this sample to a number of
- 2 discrete reaction samples, where the number of reaction samples is
- 3 selected to give a statistically significant result for the number of
- 4 copies of a target in the DNA molecules. . . .
- 5 3. Detecting the presence of the target in the DNA in a large number
- 6 of reaction samples, preferably with a sequence specific technique
- 7 such as highly multiplexed short read sequencing or a PCR
- 8 reaction wherein the PCR product is labeled to give a convenient
- 9 quantitative read out and
- 10 4. Quantitative analysis of the detection of the maternal and fetal
- 11 target sequences.
- 12

13 ('018 patent, Exh. 1022, at 8:33-9:6.) Thus, the '018 patent outlines the specific
14 steps one would take to perform digital analysis with a sequence specific technique
15 such as sequencing or a PCR reaction.

16 In contrast, the disclosures in the '018 patent that relate to a method of
17 random massively parallel sequencing are the mention of massively parallel
18 sequencing of randomly fragmented DNA, “products offered by Illumina,” citation
19 to Balasubramanian, and a sentence about the number of base pairs needed to
20 identify the chromosomal origin of a sequence. The '018 patent does not recite
21 specific series of steps one would take to determine whether fetal aneuploidy exists
22 using random massively parallel sequencing.

23 We find that the '018 patent fails to provide *express* “blazemarks” of a
24 method of massively parallel sequencing of DNA fragments randomly selected
25 from a mixture to determine fetal aneuploidy. *See In re Ruschig*, 379 F.2d 990,
26 994–95 (C.C.P.A. 1967) (analogizing, where the disclosure recited a list of
27 possible reactants, but failed to highlight the necessary one, that “[i]t is an old
28 custom in the woods to mark trails by making blaze marks on the trees. It is no

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1 help in finding a trail or in finding one's way through the woods where the trails
2 have disappeared— or have not yet been made, which is more like the case here—
3 to be confronted simply by a large number of unmarked trees.”)

4 E.

5 In the absence of an express written description, the '018 patent could still
6 provide a sufficient description of the claimed methods if one of ordinary skill in
7 the art would have understood from what was expressly described that the
8 inventors were in possession of the inventions. *See Fujikawa v. Wattanasin*, 93
9 F.3d 1559, 1570 (Fed. Cir. 1996) (“As the Board recognized, however, *ipsis verbis*
10 disclosure is not necessary to satisfy the written description requirement of section
11 112. Instead, the disclosure need only reasonably convey to persons skilled in the
12 art that the inventor had possession of the subject matter in question.”). Thus, we
13 look to how one of ordinary skill in the art would have understood the claims as a
14 whole. We find that the '018 patent does not describe how to analyze the data that
15 would be obtained from massively parallel sequencing to determine if fetal
16 aneuploidy is present and that, thus, one of ordinary skill in the art would not know
17 that the inventors possessed a method of determining fetal aneuploidy.

18 Quake’s claims require step d: using the data from the identified
19 chromosomes to compare an amount of a first chromosome (presumed to be
20 euploid¹ in the fetus) and to an amount of a second chromosome (suspected of
21 being aneuploid in the fetus) to determine the presence or absence of aneuploidy.
22 (Quake Clean Copy of Claims, Paper 7.) Lo argues that because the '018 patent
23 focuses on detecting aneuploidy based on a 1:1 ratio between predetermined

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1 sequences from two chromosomes, which is appropriate for digital analysis (*see*
2 '018 patent, Exh. 1022, at 21:1-45), it does not describe the considerations that
3 must be made when comparing data from massively parallel sequencing of DNA
4 fragments randomly selected. (Lo Motion 1, Paper 54, at 17:20-18:20, citing
5 Gabriel Decl., Exh. 1021, at ¶¶ 87-89; *see also* Lo Reply 1, Paper 79, at 8:26-9:2.)

6 Lo bases its argument on Dr. Gabriel's testimony that because human
7 chromosomes are not all the same size, randomly selected fragments are more
8 likely to be identified from larger chromosomes than from smaller chromosomes.
9 (Gabriel Decl., Exh. 1021, at ¶ 88.) According to Dr. Gabriel, given an equal
10 number of all chromosomes, there is a greater chance that a random fragment will
11 be from a larger chromosome than a smaller one. A method relying on random
12 massively parallel sequencing cannot rely on a 1:1 ratio of sequences because even
13 in the absence of aneuploidy, the number of random sequence reads aligning to a
14 larger chromosome versus those aligning to a smaller chromosome will always
15 result in a ratio greater than 1:1. (Gabriel Decl., Exh. 1021, at ¶ 88.) Dr. Gabriel
16 explains that instead of focusing on deviations from a 1:1 ratio, methods that use
17 massively parallel sequencing of randomly selected fragments must take into
18 consideration the size of the chromosomes before determining a ratio that
19 represents a normal number of chromosomes. (*See* Gabriel Decl., Exh. 1021, at ¶
20 89.)

21 Quake does not dispute that a random massively parallel sequencing method
22 for determining fetal aneuploidy would need to take into account the length of the
23 chromosomes being analyzed and could not be based on deviations from a 1:1

¹ The term "euploid" means the state of having normal sets of chromosomes.

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1 ratio. Instead, Quake argues that Dr. Gabriel admitted that statistical tests
2 reportedly disclosed in the '018 patent specification could be used to determine
3 aneuploidy. (Quake Opp. 1, Paper 73, at 10:12-25, citing Gabriel Depo., Exh.
4 2078, at 51:2-53:16 and 73:22-74:18; *see* Detter Decl., Exh. 2082, at ¶ 29.) We do
5 not find that the cited cross-examination refers to disclosures in the '018 patent
6 specification. Instead, Dr. Gabriel testifies about statistical methods, such as the
7 “T-test” and the “Z-test,” and how they could be used in general. (*See* Gabriel
8 Depo., Exh. 2078, at 51:2-53:16 and 73:22-74:18.) Quake also argues that Dr.
9 Gabriel testified that the fraction of a sample comprising a given chromosome is
10 consistent from individual to individual in the absence of aneuploidy. (*See* Quake
11 Opp. 1, Paper 73, at 10:18-21, citing Gabriel Depo, Exh. 2078, at 54:1-56:2.) We
12 do not find that the testimony Quake cites addresses the statistical analysis needed
13 when using sequences from chromosomes of differing lengths. None of the
14 testimony is evidence that Dr. Gabriel admitted statistical methods relying on the
15 different lengths of identified chromosomes were described in the '018 patent
16 specification.

17 Quake also argues that the evidence Lo submitted with its Priority Statement
18 (*see* Paper 52; Ex. 2074) and Lo's provisional application (Exh. 2010) contain less
19 disclosure than the Quake '018 patent about the statistical analysis used to assess
20 fetal aneuploidy. (Quake Opp. 1, Paper 73, at 4:3-10, citing Gabriel Depo., Exh.
21 2078, at 33:11-34:4 and 38:5-12.) Presumably Quake's argument is that a
22 description of the statistical analysis is not necessary because it not present in Lo's
23 other documents. This argument is not persuasive because written description

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1 support is evaluated on what is described in specification at issue. Whether or not
2 Lo's other documents provide sufficient written description is not at issue.

3 Quake argues further that Dr. Detter explained how the '018 patent discloses
4 a method that "intrinsically corrects for biases due to chromosome size by
5 comparing results from a test sample to normal samples using statistical methods,
6 such as a Student's T-test." (*See* Quake Opp. 1, Paper 73, at 3:3:3-6, citing Detter
7 Decl., Exh. 2082, at ¶¶ 13 and 29, and '018 patent, Exh. 1022, at 5:64-6:3 and
8 28:5-34.) This argument is not supported by the cited portions of the '018 patent.
9 Paragraphs 13 and 29 of Dr. Detter's declaration address Dr. Gabriel's cross-
10 examination testimony about what was known in the art of normalized frequencies,
11 chromosome size, and generalized statistical analyses. (*See* Lo Reply, Paper 79, at
12 9:8-24.) This testimony does not explain anything about the specification of the
13 '018 patent. Similarly, the portions of the '018 patent that Quake cites do not
14 mention chromosome size and do not discuss any "intrinsic correction." The
15 portions refer only to statistical significance in general (*see* '018 patent, Exh. 1022,
16 at 5:64-6:3) and to analysis based on a 1:1 ratio (*see id.* at 23:5-34).

17 Quake argues further that those of skill in the art would have known how to
18 correct for chromosome size in February 2007, relying on Dr. Gabriel's testimony.
19 (*See* Quake Opp. 1, Paper 73, at 3:11-15; citing Detter Decl., Exh. 2082, at ¶ 13,
20 and Gabriel Depo., Exh. 2078, at 34:13-35:9.) In the portion of her testimony cited
21 by Quake, Dr. Gabriel testifies that it was well known at the time how to create a
22 "normalized frequency," but her testimony is about the disclosure of Lo's priority
23 statement (Exhibit 2074), not the '018 patent. (*See* Gabriel Depo., Exh. 2078, at

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1 34:13-35:9.) Specifically, Dr. Gabriel addresses Example 3 of Exhibit 2074, which
2 provides for random sequencing and states:

3 By taking into account of the relative size of chromosome 21
4 compared with the other chromosome, one could obtain a normalized
5 frequency, within a reference range, of chromosome 21-specific
6 sequences from such a sequencing exercise. If the fetus has trisomy
7 21, then the normalized frequency of chromosome 21-derived
8 sequences from such a sequencing exercise will increase, thus allow
9 the detection of trisomy 21.

10
11 (Exh. 2074, at 11, *see* Gabriel Depo., Exh. 2078, at 34:17-19 (referring to Example
12 3 of Exh. 2074 “It actually says you've got to take into account the chromosome
13 size of things you're comparing.”).) Quake does not direct us to similar discussion
14 of “normalized frequency” in the '018 patent.

15 Quake’s argument is that those of skill in the art would have known *how* to
16 normalize the frequency of sequence reads by the size of the chromosome, but
17 Quake does not direct us to a portion of the '018 patent that describes the need to
18 do so. Accordingly, we are persuaded that one of ordinary skill in the art would
19 not have considered that the inventors of the '018 patent contemplated a method
20 requiring this statistical analysis.

21 The '018 patent specification does not provide a description of an analysis
22 that compares the amounts of the identified chromosomes determined from random
23 massively parallel sequencing data and determines the presence or absence of fetal
24 aneuploidy. In the absence of a description of such analysis, we are persuaded that
25 the express teachings in the specification about equipment useful for random
26 massively parallel sequencing and techniques for determining sequences are not
27 sufficient to demonstrate possession of the claimed method for “determining

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1 presence or absence of fetal aneuploidy in a maternal tissue sample comprising
 2 fetal and maternal genomic DNA.” Instead, the description in the ’018 patent
 3 indicates that the inventors had only “a mere wish or plan” to use this new
 4 technology in their invention. *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636
 5 F.3d 1341, 1351 (Fed. Cir. 2011); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*,
 6 119 F.3d 1559, 1566 (Fed. Cir. 1997).

7 In light of the Federal Circuit’s remand, we are persuaded that the ’018
 8 patent fails to describe the methods claimed by Quake as required under 35 U.S.C.
 9 § 112. Accordingly, after considering the Federal Circuit’s remand, we grant Lo
 10 Motion 1.

11 *III. Benefit of Quake’s earlier filing dates*

12 After review of the record on remand, it is apparent that the issue of written
 13 description support for Quake’s claims is not a threshold issue in this interference.
 14 (*Contra* Decision on Motions, Paper 258, at 2.) In this interference, Quake is
 15 patentee and Lo substantially copied its claims from Quake’s patent. (*See*
 16 Amendment in Appl. 13/070,275, filed 12 April 2012, at 4) (“Claims 24-27 have
 17 been substantially copied from U.S. Patent 8,008,018 issue August 31, 2011. . . . A
 18 request for interference pursuant to 37 C.F.R. § 41.202 will be filed at an
 19 appropriate time.”).) Whether Lo is entitled to the claims presented in this
 20 interference as the first to invent under 35 U.S.C. § 102(g) has not been
 21 determined. *See Guinn v. Kopf*, 96 F.3d 1419, 1421–22 (Fed. Cir. 1996) (“Section
 22 135 provides the basis for the Commissioner to declare an interference. Guinn does
 23 not dispute that Interference 103,096 was properly declared by the Commissioner.
 24 Section 135 also states that the Board ‘shall determine questions of priority’ after

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1 the declaration of an interference. Guinn asserts that his unilateral act of
2 disclaiming [the only patent claim corresponding to the count] can divest the Board
3 of its responsibility to determine the priority question in the interference. The
4 statute does not provide for any such divestment of jurisdiction.”)

5 To address the issue of priority, we first decide Quake Motion 1 for benefit
6 of the filing date of its prior application 11/701,686 (“the ’686 application”), and
7 provisional application 60/764,420 (“the ’420 provisional application”). (*See*
8 Quake Motion 1, Paper 69.) To be accorded benefit, Quake must show that both
9 applications meet the written description and enablement requirements of 35
10 U.S.C. § 112 for one embodiment within the scope of the Count. *See Hunt v.*
11 *Treppschuh*, 523 F.2d 1386, 1389 (C.C.P.A. 1975). The Count in this interference
12 is claim 24 of Lo’s involved application 13/070,275, which recites

13 A method for determining presence or absence of fetal
14 aneuploidy in a maternal biological sample comprising fetal and
15 maternal genomic DNA, wherein the method comprises:
16 a. obtaining a mixture of fetal and maternal genomic DNA from
17 said maternal biological sample;
18 b. conducting massively parallel DNA sequencing of DNA
19 fragments randomly selected from the mixture of fetal and maternal
20 genomic DNA of step a) to determine the sequence of said DNA
21 fragments;
22 c. identifying chromosomes to which the sequences obtained in
23 step b) belong;
24 d. using data of step c) to compare an amount of at least one
25 first chromosome in said mixture of maternal and fetal genomic DNA
26 to an amount of at least one second chromosome in said mixture of
27 maternal and fetal genomic DNA, wherein said at least one first
28 chromosome is presumed to be euploid in the fetus, wherein said at
29 least one second chromosome is suspected to be aneuploid in the

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1 fetus, thereby determining the presence or absence of said fetal
2 aneuploidy.

3

4 (Decl., Paper 1, at 4.) The Count is almost identical to claim 1 of Quake's '018
5 patent, including the limitation to "conducting massively parallel DNA sequencing
6 of DNA fragments randomly selected from a mixture of fetal and maternal
7 genomic DNA" to compare amounts of two chromosomes and determine the
8 presence or absence of fetal aneuploidy.

9 Quake argues that step d. of the Count, using the data from chromosomes
10 identified in random massively parallel sequencing to compare an amount of at
11 least a first and second chromosome to determine fetal aneuploidy, is supported by
12 paragraphs 27, 59, 95, 99, 104, and 141-149 of the '686 application (Exh. 2004)
13 and paragraphs 21, 37, 50-52, 81, and 89-90 of the '420 provisional application
14 (Exh. 2005). (Quake Motion 1, Paper 69, at 7:4-12, citing Detter Decl., Exh. 2049,
15 at ¶ 100.) Quake cites to the testimony of Dr. Detter in support of its argument, but
16 neither Quake nor Dr. Detter explain how these paragraphs support the element of
17 the Count.

18 Lo argues that the cited paragraphs of the '686 application and '420
19 provisional application do not support an embodiment of the Count because they
20 disclose a statistical method for detecting aneuploidy based on a 1:1 ratio between
21 predetermined target sequences on two chromosomes. (See Lo Opp. 1. Paper 71, at
22 18:2-5.) Similar to its argument that the '018 patent lacks written description for
23 Quake's claims, Lo argues that the random sequencing and alignment method of
24 the Count does not require deviation from a 1:1 ratio to detect aneuploidy. (See Lo
25 Opp. 1. Paper 71, at 18:14-16.) Lo argues that the data analysis used in the

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1 example at paragraphs 141-149 of the '686 application relies on detecting variation
2 from a 1:1 ratio between predetermined sequences, which would not work for a
3 random sequencing and alignment method of the Count. (Lo Opp. 1, Paper 71, at
4 18:24-27, *see* Gabriel Decl, Exh. 1021, at ¶¶ 88 and 89 (cited in Lo Material Fact
5 117).)

6 As explained above, we are persuaded by Dr. Gabriel's testimony that
7 deviations from a 1:1 ratio of identified sequences is not an appropriate analysis for
8 a method of detecting aneuploidy using random sequencing of a mixture of
9 maternal and fetal genomic DNA because the sequence reads must be normalized
10 to chromosome size. Although Quake argues that its prior applications describe
11 the use of a t statistic in its analysis to measure statistical significance (*see* Quake
12 Reply 1, Paper 81, at 4:11-18²), we are not persuaded that this aspect of statistical
13 analysis describes an analysis other than reliance on deviations from a 1:1 ratio and
14 normalization to chromosome size. Instead, we are persuaded that the statistical
15 analysis described in the prior applications does not recognize the need to
16 normalize the number of sequence reads to the size of the chromosomes from
17 which they are derived.

18 Accordingly, we are not persuaded that the '686 application and '420
19 provisional application present written description of an embodiment of the Count.

² Quake cites to the Board's Decision to Institute in IPR2013-00390 in support of its argument. (*See* Quake Reply 1, Paper 81, at 4:11-18, citing Ex. 2094 at 20:3-13.) IPR2013-00390 addressed the patentability of Patent 8,195,415, which was filed later than and does not share a specification with Quake's '686 application. Quake does not sufficiently explain how decisions or findings of fact made in IPR2013-00390 are specifically relevant to the issues of this interference.

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1 To be a constructive reduction to practice of a count, an application must be a
2 described and enabled anticipation under 35 U.S.C. 102(g)(1) of the subject matter
3 of a count. *See* 37 C.F.R. § 41.201. Thus, neither the '686 application nor the '420
4 provisional application is a constructive reduction to practice of the Count.
5 Accordingly, we deny Quake Motion 1 as to both of these prior applications.

6 *IV. Conclusion*

7 We grant Lo Motion 1, determining that Quake's involved claims are not
8 patentable. Quake's claims will be canceled when judgment is entered in this
9 proceeding.

10 We deny Quake Motion 1 to be accorded the benefit of the filing dates of its
11 earlier applications as constructive reductions to practice of the Count.

12 An Order to Show Cause is issued separately regarding continuation of the
13 interference to a priority phase. (*See* Paper 274.)

14 Any request for rehearing of our decisions filed 18 January 2018 will be
15 considered timely. 37 C.F.R. § 41.104(b).

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

YUK-MING DENNIS **LO**, ROSSA WAI KWUN CHIU, and KWAN CHEE
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(Application 12/178,181; 13/070,240; 12/614,350; and 13/070,251),

v.

STEPHEN **QUAKE** and HEI-MUN CHRISTINA FAN

Senior Party

(Application 12/393,833).

Patent Interference No. 105,923 (DK)
(Technology Center 1600)

Judgment

37 C.F.R. § 41.127

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

KATZ, *Administrative Patent Judge*.

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1 Following remand from the Federal Circuit (*see The Board of Trustees of the*
2 *Leland Stanford Junior University v. The Chinese University of Hong Kong*, App.
3 2015-011 (Fed. Cir. June 27, 2017)), we determine that application 12/393,833
4 fails to provide written description of Quake's involved, copied claims as required
5 by 35 U.S.C. § 112. (*See* Decision on Motions, Paper 247.) Accordingly, we grant
6 Lo Motion 1. We need not determine whether the benefit accorded to Quake upon
7 declaration should be changed, as argued in Lo Motion 5 and Quake Motion 1.

8 ORDERED that judgment be entered against Quake for Count 1 (*see* Paper
9 1);

10 FURTHER ORDERED that claims 25, 29, 32, 40, 42, 78, 79, 86, 87, 90, 91,
11 93, 95, 97, and 98-101 of Quake's involved application 12/393,833 be FINALLY
12 REFUSED 35 U.S.C. 135(a);

13 FURTHER ORDERED that a copy of this judgment be entered in the
14 administrative records of the involved 12/393,833 application and Lo applications
15 12/178,181, 13/070,240, 12/614,350, and 13/070,251.

16 FURTHER ORDERED that a party seeking judicial review timely serve
17 notice on the Director of the United States Patent and Trademark Office. 37 C.F.R.
18 §§ 90.1 and 104.2.

19 FURTHER ORDERED that the parties are directed to 35 U.S.C. § 135(c)
20 and to 37 C.F.R. § 41.205 regarding the filing of settlement agreements.

Interference 105,923

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Filed: December 20, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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Junior Party

(Application 12/178,181; 13/070,240; 12/614,350; and 13/070,251),

v.

STEPHEN **QUAKE** and HEI-MUN CHRISTINA FAN

Senior Party

(Application 12/393,833).

Patent Interference No. 105,923 (DK)
(Technology Center 1600)

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 105,923 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 233; *see* Decision on Motion, Paper 232.)

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].”).) Indeed, the passage quoted above expressly discloses massively
23 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 Detter, 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, at ¶ 58; *see Detter*
 19 *Decl. Exh. 2049*, at ¶ 91; *see also Board of Trustees*, at slip op. 6.) Lo also agrees
 20 that it was known that Illumina products could perform massively parallel
 21 sequencing of randomly selected DNA fragments. (See Lo Motion 1, Paper 26, at
 22 23:17-19, Material Fact 50 (“Illumina sequencing platforms can perform either
 23 random or targeted DNA sequencing, depending on whether predetermined target
 24 DNA 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 54, 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 9:25-10:13.)

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 7:8-
12 18.) 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-18, 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® 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 4:23-25.) 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 4:25-5:2; *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 4:26-27, 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 11:21-12:19.) 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 9:22-10:9.)

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 54, 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 10:11-25, 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 10:18-20, 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 4:4-12, 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 54, 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”). Lo’s '181 application was published on 29 January 2009, as U.S.

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

7 Because Quake's involved application does not provide a sufficient written
8 description to support the claims that "tracked" Lo's claims, Quake's claims are
9 unpatentable to Quake and Quake should not have been able to challenge Lo's
10 claims with them. Accordingly, Quake does not have standing in this proceeding
11 and we determine that the written description of Quake's claims is a threshold
12 issue. (*See* 37 C.F.R. § 41.201 (defining "threshold issue" as one which, if
13 resolved in favor of the movant, would deprive the opponent of standing in the
14 interference, for example, unpatentability for lack of written description under 35
15 U.S.C. § 112 of an involved application where the applicant's claims were first
16 made after the publication of a movant's application and the applicant could have
17 suggested an interference).)

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

Interference 105,923

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Filed: December 20, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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).

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

Judgment

37 C.F.R. § 41.127

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

KATZ, *Administrative Patent Judge*.

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1 Following remand from the Federal Circuit (*see The Board of Trustees of the*
2 *Leland Stanford Junior University v. The Chinese University of Hong Kong*, App.
3 2015-011 (Fed. Cir. June 27, 2017)), we determine that application 12/393,833 fails to
4 provide written description of Quake's involved, copied claims as required by 35
5 U.S.C. § 112. (*See* Decision on Motions, Paper 245.) Accordingly, we grant Lo
6 Motion 1. We need not determine whether the benefit accorded to Quake upon
7 declaration should be changed, as argued in Lo Motion 5 and Quake Motion 1.

8 ORDERED that judgment be entered against Quake for Count 1 (*see* Paper
9 1);

10 FURTHER ORDERED that claims 25, 29, 32, 40, 42, 78, 79, 86, 87, 90, 91,
11 93, 95, 97, and 98-101 of Quake's involved application 12/393,833 be FINALLY
12 REFUSED 35 U.S.C. 135(a);

13 FURTHER ORDERED that a copy of this judgment be entered in the
14 administrative records of the involved 12/393,833 application and Lo application
15 13/417,119.

16 FURTHER ORDERED that a party seeking judicial review timely serve
17 notice on the Director of the United States Patent and Trademark Office. 37 C.F.R.
18 §§ 90.1 and 104.2.

19 FURTHER ORDERED that the parties are directed to 35 U.S.C. § 135(c)
20 and to 37 C.F.R. § 41.205 regarding the filing of settlement agreements.

Interference 105,924

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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).

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

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 Detter, 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[®] 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.¹

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).)

¹ 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.

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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.

3

4

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