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Paper 7
Entered: December 9, 2013

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SEQUENOM, INC.
Petitioner

v.

THE BOARD OF TRUSTEES OF
THE LELAND STANFORD JUNIOR UNIVERSITY
Patent Owner

Case IPR2013-00390
Patent 8,195,415 B2

Before LORA M. GREEN, FRANCISCO C. PRATS, and SCOTT E. KAMHOLZ, *Administrative Patent Judges.*

PRATS, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

A. Statement of the Case

On June 26, 2013, Sequenom, Inc. ("Sequenom") filed a petition ("Pet.") to institute an *inter partes* review of claims 1-17, all of the claims, of U.S. Patent No. 8,195,415 B2 (Ex. 1001, "the '415 patent"). Paper 1. Patent Owner, The Board of Trustees of the Leland Stanford Junior University ("Stanford"), did not file a Preliminary Response. We have jurisdiction under 35 U.S.C. §§ 6(b) and 314.

The standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which states:

> THRESHOLD. -- The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

Sequenom has persuaded us that it has shown, under 35 U.S.C. § 314(a), that there is a reasonable likelihood that it would prevail with respect to at least one of the claims challenged in its petition. Accordingly, for the reasons below, we grant the petition and institute an *inter partes* review of claims 1-17.

B. Related Proceedings

The '415 patent is asserted in co-pending litigation captioned as *Verinata Health, Inc. and the Board of Trustees of the Leland Stanford Junior University v. Sequenom, Inc. and Sequenom Center for Molecular Medicine LLC*, United States District Court for the Northern District of California, Case No. 3:12-cv-00865-SI. Pet. 1. The '415 patent is involved also in Interference No. 105,922, declared on May 3, 2013. *Id.*

C. Proposed Grounds of Unpatentability

Sequenom contends that the challenged claims are unpatentable under 35 U.S.C. §§ 102 and/or 103 on the following specific grounds (Pet. 3-60):[1]

Reference[s]	**Basis**	**Claims challenged**
Lo II[2]	§ 102(e)	1-6, 8-12
Lo II, Hillier,[3] Smith[4]	§ 103	7
Lo II, Wang[5]	§ 103	13, 16
Lo II, Shimkets,[6] Dohm[7]	§ 103	14
Lo II, Quake[8]	§ 103	15
Lo II, Wang, Hillier, Smith	§ 103	17
Lo II, Wang	§ 103	1-6, 8-12

[1] Petitioner supports its challenge with a declaration, executed Jun. 26, 2013, by Stacey Bolk Gabriel (Ex. 1010).
[2] Lo et al., U.S. Patent App. Pub. No. 2009/0029377 A1 (filed Jul. 23, 2008) (Ex. 1002).
[3] LaDeana W. Hillier et al., *Whole-genome sequencing and variant discovery in C. elegans*, 5 NATURE METHODS 183-188 (published online Jan. 20, 2008) (Ex. 1006).
[4] Andrew D. Smith et al., *Using quality scores and longer reads improves accuracy of Solexa read mapping*, 9 BMC BIOINFORMATICS 128 (Feb. 28, 2008) (Ex. 1009).
[5] Tian-Li Wang et al., *Digital karyotyping*, 99 PNAS 16156-16161 (Dec. 10, 2002) (Ex. 1005).
[6] Shimkets et al., U.S. Patent App. Pub. No. 2005/0221341 A1 (published Oct. 6, 2005) (Ex. 1004).
[7] Juliane C. Dohm et al., *Substantial biases in ultra-short read data sets from high-throughput DNA sequencing*, 36 NUCL. ACIDS RES. e105 (published online Jul. 26, 2008) (Ex. 1007).
[8] Quake et al., U.S. Patent No. 7,888,017 B2 (filed Feb. 2, 2007) (Ex. 1008).

Lo II, Wang, Hillier, Smith	§ 103	7
Lo II, Wang, Shimkets, Dohm	§ 103	14
Lo II, Wang, Quake	§ 103	15
Lo I,[9] Shimkets	§ 103	1-6, 8-12
Lo I, Shimkets, Hillier, Smith	§ 103	7
Lo I, Shimkets, Wang	§ 103	13, 16
Lo I, Shimkets, Dohm	§ 103	14
Lo I, Shimkets, Quake	§ 103	15
Lo I, Shimkets, Wang, Hillier, Smith	§ 103	17

D. The '415 Patent

The '415 patent describes prenatal genetic diagnosis methods that allow detection of chromosomal aberrations, without the use of invasive techniques such as amniocentesis or chorionic villus sampling, which pose potentially significant risks to both fetus and mother. *See* Ex. 1001, col. 1, ll. 30-54. In particular, the '415 patent discloses that fetal DNA can constitute nearly ten percent of the cell-free DNA in maternal plasma, and, therefore, fetal aneuploidy can be detected by determining the sequences of the DNA fragments in the maternal plasma. *See id.* at col. 1, l. 55-col. 2, l. 24. The '415 patent thus describes "the successful use of shotgun sequencing and mapping of DNA to detect fetal trisomy 21 (Down syndrome), trisomy 18 (Edward syndrome), and trisomy 13 (Patau syndrome),

[9] Lo I, et al., U.S. Provisional Patent Application 60/951,438 (filed July 23, 2007) (Ex. 1003).

carried out non-invasively using cell-free fetal DNA in maternal plasma." *Id.* at col. 4, ll. 17-21.

To perform these analyses, the sequences of the DNA fragments in a maternal plasma sample are determined by generating sequence tags of sufficient length "to be assigned to a chromosomal location with a genome and of a sufficient number to reflect abnormal distribution." *Id.* at col. 4, ll. 38-40. Once the sequence tags are assigned to their chromosomal locations in a reference genome, "[o]ne then may determine a first number of sequence tags mapped to at least one normally distributed chromosome portion and a second number of sequence tags mapped to the specified chromosome portion [suspected of abnormal distribution], both chromosomes being in one mixed sample." *Id.* at col. 4, ll. 46-50. After correcting for "nonuniform distribution [of] sequence tags to different chromosomal portions[,]" *id.* at col. 4, ll. 51-52, a differential is calculated "between the first number and the second number which is determinative of whether or not the abnormal distribution exists." *Id.* at col. 4, ll. 64-67.

The '415 patent explains that the methods do not require sequence differentiation between fetal and maternal DNA, "because the summed contribution of both maternal and fetal sequences in a particular chromosome or chromosome portion will be different as between an intact, diploid chromosome and an aberrant chromosome, i.e., with an extra copy, missing portion or the like." *Id.* at col. 3, ll. 56-62. That is, "the method does not rely on a priori sequence information that would distinguish fetal DNA from maternal DNA." *Id.* at col. 3, ll. 62-64.

Claims 1 and 13, the independent claims of the '415 patent, are reproduced below:

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