United States Court of Appeals for the Federal Circuit

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,
Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,
Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,
Defendants-Appellants

ISIS INNOVATION LIMITED,
Defendant

2014-1139, 2014-1144

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

Decided: June 12, 2015

DAVID ISAAC GINDLER, Irell & Manella LLP, Los Angeles, CA, argued for plaintiff-appellee Ariosa Diagnostics, Inc. Also represented by ANDREI IANCU; AMIR NAINI, Russ August & Kabat, Los Angeles, CA.

WILLIAM PAUL SCHUCK, Bartko, Zankel, Bunzel & Miller, San Francisco, CA, for plaintiff-appellee Natera, Inc., counterclaim defendant-appellee DNA Diagnostics Center, Inc.

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KEVIN EDWARD NOONAN, McDonnell, Boehnen Hulbert & Berghoff, LLP, Chicago, IL, for amicus curiae Biotechnology Industry Organization.

WILLIAM LARRY RESPESS, I, Sheppard, Mullin, Richter, & Hampton LLP, San Diego, CA, for amicus curiae The San Diego Intellectual Property Law Association.

Before REYNA, LINN, and WALLACH, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge* REYNA.

Concurring Opinion filed by *Circuit Judge* LINN.

REYNA, *Circuit Judge.*

This appeal is from a grant of summary judgment of invalidity of the asserted claims of U.S. Patent No. 6,258,540 ("the '540 patent"). The United States District Court for the Northern District of California found that the asserted claims of the '540 patent are not directed to patent eligible subject matter and are therefore invalid under 35 U.S.C. § 101. For the reasons explained below, we *affirm*.

I

In 1996, Drs. Dennis Lo and James Wainscoat discovered cell-free fetal DNA ("cffDNA") in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste. cffDNA is non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman. Applying a combination of known laboratory techniques to their discovery, Drs. Lo and Wainscoat implemented a method for detecting the small fraction of paternally inherited cffDNA in maternal plasma or serum to determine fetal characteristics, such as gender. The invention, commercialized by Sequenom as its MaterniT21 test, created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques that took samples from the fetus or placenta. In 2001, Drs. Lo and Wainscoat obtained the '540 patent, which relates to this discovery.

The parties agree that the patent does not claim cffDNA or paternally inherited cffDNA. Instead, the '540 patent claims certain methods of using cffDNA. The steps of the method of claim 1 of the '540 patent include amplifying the cffDNA contained in a sample of a plasma or serum from a pregnant female and detecting the paternally inherited cffDNA. Amplifying cffDNA results in a single copy, or a few copies, of a piece of cffDNA being multiplied across several orders of magnitude, generating thousands to millions of copies of that particular DNA sequence. In the amplification step, DNA is extracted from the serum or plasma samples and amplified by polymerase chain reaction ("PCR") or another method. PCR exponentially amplifies the cffDNA sample to detectable levels.

In the detecting step, the lab technician adds the amplified cffDNA to an agarose gel containing ethidium

bromide to stain and visualize the paternally inherited cffDNA.

The '540 patent also provides for making a diagnosis of certain fetal characteristics based on the detection of paternally inherited cffDNA. The specification explains that analysis of cffDNA permits more efficient determination of genetic defects and that a pregnant woman carrying a fetus with certain genetic defects will have more cffDNA in her blood than will a woman with a normal fetus. '540 patent col. 3 ll. 30-43.

Claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent are at issue in this appeal.[1] Independent claim 1 requires:

> 1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises
>
> amplifying a paternally inherited nucleic acid from the serum or plasma sample and
>
> detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

'540 patent col. 23 l. 61-67.

For comparison, independent claims 24 and 25 require:

> 24. A method for detecting a paternally inherited nucleic acid on a maternal blood sample, which method comprises:

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[1] The parties have stipulated that for the purposes of this appeal claims 1, 2, 4, 5, 8, 9-22, 24 and 25 are representative of claims 6, 7, 12, 13, 15, and 18 of the '540 patent. J.A. 24-25, 30-31.

> removing all or substantially all nucleated and anucleated cell populations from the blood sample,
>
> amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid to a test for the Paternally [sic] inherited fetal nucleic acid.
>
> 25. A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises
>
> obtaining a non-cellular fraction of the blood sample
>
> amplifying a paternally inherited nucleic acid from the non-cellular fraction
>
> and performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Id. at 26 ll. 20-36.

The remaining claims explain how the method of detection occurs or how it can be used. For example, claim 2 depends from claim 1 and claims amplification by polymerase chain reaction. *Id.* at col. 24 ll. 60-61. Claim 4 similarly depends from claim 1 and claims detection via a sequence specific probe. *Id.* col. 24 ll. 65-67. Claim 21 also depends from claim 1, but instead of focusing solely on a method for detecting, it focuses on a method for performing a prenatal diagnosis, using claim 1's method for detecting. *Id.* col. 26 ll. 4-14.

II

Appellee Ariosa Diagnostics, Inc. (formerly known as "Aria Diagnostics, Inc.") makes and sells the Harmony Test, a non-invasive test used for prenatal diagnosis of certain fetal characteristics. Natera, Inc. makes and sells

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