

**United States Court of Appeals  
for the Federal Circuit**

---

**ARIOSIA 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.

MICHAEL J. MALECEK, Kaye Scholer LLP, Palo Alto, CA, argued for defendants-appellants. Also represented by PETER E. ROOT, Menlo Park, CA; ATON ARBISSER, Los Angeles, CA.

RICHARD L. BLAYLOCK, Pillsbury Winthrop Shaw Pittman LLP, San Diego, CA, for amicus curiae Invitae Corporation. Also represented by KIRKE M. HASSON, COLIN TRAVERS KEMP, San Francisco, CA.

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.<sup>1</sup> 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:

---

<sup>1</sup> 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

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.