UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Plaintiffs,

09 Civ. 4515

-against-

OPINION

UNITED STATES PATENT AND TRADEMARK OFFICE, ET AL.,

Defendants.

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Sweet, D.J.

Plaintiffs Association for Molecular Pathology, et al. (collectively "Plaintiffs") have moved for summary judgment pursuant to Rule 56, Fed. R. Civ. P., to declare invalid fifteen claims (the "claims-in-suit") contained in seven patents (the "patents-in-suit") relating to the human *BRCA1* and *BRCA2* genes (Breast Cancer Susceptibility Genes 1 and 2) (collectively, "*BRCA1/2*") under each of (1) the Patent Act, 35 U.S.C. § 101 (1952), (2) Article I, Section 8, Clause 8 of the United States Constitution, and (3) the First and Fourteenth Amendments of the Constitution because the patent claims cover products of nature, laws of nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought. The defendant United States Patent and Trademark Office ("USPTO") issued the patents-in-suit which are held by defendants Myriad Genetics and the University of Utah Research Foundation ("UURF") (collectively "Myriad" or the "Myriad Defendants"). Myriad has cross-moved under Rule 56, Fed. R. Civ. P., for summary judgment dismissing Plaintiffs' complaint, and the USPTO has cross-moved under Rule 12(c), Fed. R. Civ. P., for judgment on the pleadings. Based upon the findings and conclusions set forth below, the motion of Plaintiffs to

declare the claims-in-suit invalid is granted, the cross-motion of Myriad is denied, and the motion of the USPTO is granted.

As discussed infra in greater detail, the challenged patent claims are directed to (1) isolated DNA containing all or portions of the *BRCA1* and *BRCA2* gene sequence and (2) methods for "comparing" or "analyzing" *BRCA1* and *BRCA2* gene sequences to identify the presence of mutations correlating with a predisposition to breast or ovarian cancer. Plaintiffs' challenge to the validity of these claims, and the arguments presented by the parties and amici, have presented a unique and challenging question:

> Are isolated human genes and the comparison of their sequences patentable?

Two complicated areas of science and law are involved: molecular biology and patent law. The task is to seek the governing principles in each and to determine the essential elements of the claimed biological compositions and processes and their relationship to the laws of nature. The resolution of the issues presented to this Court deeply

concerns breast cancer patients, medical professionals, researchers, caregivers, advocacy groups, existing gene patent holders and their investors, and those seeking to advance public health.

The claims-in-suit directed to "isolated DNA" containing human *BRCA1/2* gene sequences reflect the USPTO's practice of granting patents on DNA sequences so long as those sequences are claimed in the form of "isolated DNA." This practice is premised on the view that DNA should be treated no differently from any other chemical compound, and that its purification from the body, using well-known techniques, renders it patentable by transforming it into something distinctly different in character. Many, however, including scientists in the fields of molecular biology and genomics, have considered this practice a "lawyer's trick"[1] that circumvents the prohibitions on the direct patenting of the DNA in our bodies but which, in practice, reaches the same result. The resolution of these motions is based upon long recognized principles of molecular biology and genetics: DNA represents the physical embodiment of biological information, distinct in its

[1] See, e.g., John M. Conley & Roberte Markowski, Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents, 85 J. Pat. & Trademark Off. Soc'y 301, 305 (2003).

essential characteristics from any other chemical found in nature. It is concluded that DNA's existence in an "isolated" form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes. Therefore, the patents at issue directed to "isolated DNA" containing sequences found in nature are unsustainable as a matter of law and are deemed unpatentable subject matter under 35 U.S.C. § 101.

Similarly, because the claimed comparisons of DNA sequences are abstract mental processes, they also constitute unpatentable subject matter under § 101.

The facts relating to molecular biology are fundamental to the patents at issue and to the conclusions reached. Consequently, in the findings which follow, the discussion of molecular biology precedes the facts concerning the development, application, and description of the patents. Following those facts are the conclusions which compel the partial grant of summary judgment to the Plaintiffs, the denial of Myriad's cross-motion, and the grant of the USPTO's motion for judgment on the pleadings.

I. PRIOR PROCEEDINGS

The complaint in this action was filed on May 12, 2009, alleging violations of 35 U.S.C. § 101; Article I, Section 8, Clause 8 of the United States Constitution; and the First and Fourteenth Amendments to the Constitution.

Defendants moved to dismiss the complaint which motion was denied by the opinion of November 1, 2009. See Assoc. for Molecular Pathology v. U.S. Patent and Trademark Office, 669 F. Supp. 2d 365 (S.D.N.Y. 2009). Plaintiffs were found to have the necessary standing to assert their declaratory judgment claims against the Myriad Defendants and the USPTO, and specific personal jurisdiction was found to exist over the Directors of the UURF by virtue of acts performed in their official capacity that were directed to the state of New York. It was also determined that this Court possessed the necessary subject matter jurisdiction to hear Plaintiffs' constitutional claims against the USPTO and that the complaint satisfied the pleading requirements set forth in Ashcroft v. Iqbal, 129 S. Ct. 1937 (2009).

Plaintiffs' motion for summary judgment and the cross-motions for summary judgment and judgment on the pleadings were heard and marked fully submitted on February 4, 2010.

II. THE PARTIES AND AMICI

Plaintiff Association for Molecular Pathology ("AMP") is a not-for-profit scientific society dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of genomics and proteomics. AMP members participate in basic and translational research aimed at broadening the understanding of gene/protein structure and function, disease processes, and molecular diagnostics, and provide clinical medical services for patients, including diagnosis of breast cancer. Sobel Decl. ¶¶ 2, 4-5.[2]

Plaintiff the American College of Medical Genetics ("ACMG") is a private, non-profit voluntary organization of clinical and laboratory geneticists. The

[2] For purposes of this opinion, references to the parties' declarations will be in the format [Declarant name] Decl. ¶ [paragraph number].

Fellows of the ACMG are doctoral level medical geneticists and other physicians involved in the practice of medical genetics. With more than 1300 members, the ACMG's mission is to improve health through the practice of medical genetics. In order to fulfill this mission, the ACMG strives to define and promote excellence in medical genetics practice and the integration of translational research into practice; promote and provide medical genetics education; increase access to medical genetics services and integrate genetics into patient care; and advocate for and represent providers of medical genetics services and their patients. Watson Decl. ¶¶ 2, 4-5.

Founded in 1922, plaintiff the American Society for Clinical Pathology ("ASCP") is the largest and oldest organization representing the medical specialty of pathology and laboratory medicine. ASCP is a not-for-profit entity organized for scientific and educational purposes and dedicated to patient safety, public health, and the practice of pathology and laboratory medicine and has 130,000 members working as pathologists and laboratory professionals. ASCP members design and interpret the tests that detect disease, predict outcome, and determine the appropriate therapy for the patient. The ASCP is

recognized for its excellence in continuing professional education, certification of laboratory professionals, and advocacy. Ball Decl. ¶¶ 2, 5.

Plaintiff the College of American Pathologists ("CAP") is a national medical society representing more than 17,000 pathologists who practice anatomic pathology and laboratory medicine in laboratories worldwide. The College's Commission on Laboratory Accreditation is responsible for accrediting more than 6,000 laboratories domestically and abroad, and approximately 23,000 laboratories are enrolled in CAP's proficiency testing programs. It is the world's largest association composed exclusively of board-certified pathologists and pathologists in training worldwide and is widely considered the leader in laboratory quality assurance. CAP is an advocate for high quality and cost-effective medical care. Scott Decl. ¶¶ 2, 4-5.

Plaintiff Haig Kazazian, M.D. ("Dr. Kazazian"), is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. He is a human genetics researcher and the previous chair of the Department. Dr.

Kazazian and plaintiff Arupa Ganguly, Ph.D. ("Dr. Ganguly"), designed tests to screen the *BRCA1* and *BRCA2* genes in their lab and provided screening to approximately 500 women per year starting in 1996. Drs. Kazazian and Ganguly ceased their *BRCA1/2* testing in response to cease-and-desist letters from Myriad relating to the patents-in-suit. Kazazian Decl. ¶¶ 1-5.

Plaintiff Dr. Ganguly is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Dr. Ganguly's work previously included *BRCA1/2* screening for both research and clinical purposes. She ceased *BRCA1/2* screening following her receipt of cease-and-desist letters from Myriad accusing her lab of violating the patents-in-suit. Ganguly Decl. ¶¶ 1, 3-5.

Plaintiff Wendy Chung, M.D., Ph.D. ("Dr. Chung"), is an Associate Professor of Pediatrics and the Herbert Irving Professor of Pediatrics and Medicine in the Division of Molecular Genetics at Columbia University. Dr. Chung is a human geneticist whose current research includes research on the *BRCA1* and *BRCA2* genes. Because of the patents-in-suit, Dr. Chung currently cannot tell research subjects in

her studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA1/2* testing services. Chung Decl. ¶¶ 1-9, 11-13, 16.

Plaintiff Harry Ostrer, M.D. ("Dr. Ostrer"), is a Professor of Pediatrics, Pathology and Medicine and Director of the Human Genetics Program in the Department of Pediatrics at New York University School of Medicine. Dr. Ostrer's work has focused on understanding the genetic basis of development and disease, including disorders of sexual differentiation and genetic susceptibility to breast and prostate cancer and malignant melanoma. Dr. Ostrer is actively engaged in identifying genes that convey risk of breast cancer and that may mitigate the effects of mutations in the *BRCA1* and *BRCA2* genes. Dr. Ostrer is also the Director of the Molecular Genetics Laboratory of NYU Medical Center, one of the largest academic genetic testing laboratories in the United States. Because of the patents-in-suit, Dr. Ostrer currently cannot tell research subjects in his studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA1/2* testing services. Ostrer Decl. ¶¶ 1-4.

Plaintiff David Ledbetter, Ph.D. ("Dr.

Ledbetter"), is a Professor of Human Genetics and Director of the Division of Medical Genetics at the Emory University School of Medicine. Research in his laboratory focuses on the molecular characterization of human developmental disorders. Dr. Ledbetter directs the Emory Genetics Laboratory which provides testing services for individuals with or at risk for genetic diseases. Because of the patents-in-suit, Dr. Ledbetter cannot offer comprehensive *BRCA1/2* genetic testing to patients. Ledbetter Decl. ¶¶ 1-8, 16.

Plaintiff Stephen T. Warren, Ph.D. ("Dr. Warren"), is the William Patterson Timmie Professor of Human Genetics, Chairman of the Department of Human Genetics, and Professor of Biochemistry and Professor of Pediatrics at Emory University. He is a past President of the American Society of Human Genetics. Dr. Warren supervises genetic research at Emory and is responsible for the laboratories at the Emory Genetics Laboratory. These laboratories would offer *BRCA1/2* genetic testing but for the patents-in-suit. Ledbetter Decl. ¶¶ 1, 16.

Plaintiff Ellen Matloff, M.S. ("Ms. Matloff"), is Director of the Yale Cancer Genetic Counseling Program.

Ms. Matloff advises women on the desirability of obtaining an analysis of their genes to determine if the women have the genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. If she determines that such an analysis is warranted and the individual woman concurs, Ms. Matloff arranges for the analysis and then advises the woman of the significance of the results. Ms. Matloff would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. Matloff Decl. ¶¶ 1-4, 11.

Plaintiff Elsa W. Reich, M.S. ("Ms. Reich"), is a Professor in the Department of Pediatrics at New York University. She is a genetic counselor. She helps women decide whether to be tested for mutations in the *BRCA1* and *BRCA2* genes. If they need testing, she sends samples to Myriad and explains the results for the women. Ms. Reich would like to have the option to send patient samples to laboratories other than Myriad for *BRCA1/2* sequencing. Reich Decl. ¶¶ 1-3, 8.

Plaintiff Breast Cancer Action ("BCA") is a national organization of approximately 30,000 members based in San Francisco, California. BCA is dedicated to

representing the voices of people affected by breast cancer in order to inspire and compel the changes necessary to end the breast cancer epidemic. Its members include breast cancer survivors, family members of people diagnosed with breast cancer and other people affected by or concerned about breast cancer. BCA advocates for policy changes directed at achieving prevention, finding better treatments, and reducing the incidence of breast cancer, provides information about breast cancer to anyone who needs it via newsletters, web sites, e-mail and a toll-free number, and organizes people to get involved in advocacy to advance its policy goals. Brenner Decl. ¶¶ 1-3.

Plaintiff Boston Women's Health Book Collective, doing business as Our Bodies Ourselves ("OBOS"), is a non-profit, public interest women's health education, advocacy, and consulting organization. OBOS provides information about health, sexuality and reproduction from a feminist and consumer perspective. OBOS advocates for women's health and provides information to members of the public about genetic analysis. Norsigian Decl. ¶¶ 1-4.

Plaintiff Lisbeth Ceriani ("Ms. Ceriani") is a 43-year-old single mother who was diagnosed with cancer in

both breasts in May 2008. Ms. Ceriani is insured through MassHealth, a Medicaid insurance program for low-income people. Her oncologist and genetic counselor recommended that she obtain *BRCA1* and *BRCA2* genetic testing because she may need to consider further surgery in order to reduce her risk of ovarian cancer. However, Myriad will not accept the MassHealth coverage, and Ms. Ceriani is unable to pay the full cost out-of-pocket. Ceriani Decl. ¶¶ 1-6.

Plaintiff Runi Limary ("Ms. Limary") is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in 2005. Ms. Limary obtained *BRCA1/2* testing through Myriad and received the following result: "genetic variant of uncertain significance." Because of Myriad's patents, she is unable to pursue alternative testing options. Limary Decl. ¶¶ 1-5.

Plaintiff Genae Girard ("Ms. Girard") is a 39-year-old woman who was diagnosed with breast cancer in 2006. Shortly after her diagnosis, she obtained *BRCA1/2* genetic testing from Myriad and tested positive for a deleterious mutation on the *BRCA2* gene. She sought a second opinion of that test result but learned that Myriad is the only laboratory in the country that can provide full

BRCA1/2 sequencing. Girard Decl. ¶¶ 1-6.

Plaintiff Patrice Fortune ("Ms. Fortune") is a 48-year-old woman who was diagnosed with breast cancer in February 2009. Ms. Fortune is insured through Medi-Cal. Her oncologist and genetic counselor recommended that she obtain *BRCA1/2* genetic testing, including the supplemental testing that is offered by Myriad separate from its standard test, but told her that Myriad would not accept her insurance. Ms. Fortune is unable to pay the full cost out-of-pocket. Fortune Decl. ¶¶ 1-5.

Plaintiff Vicky Thomason ("Ms. Thomason") is a 52-year-old woman who was diagnosed with ovarian cancer in 2006. She obtained *BRCA1/2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA1/2* genetic testing offered by Myriad that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that her insurance would not cover the full cost of that test. Ms. Thomason is unable to afford the extra cost. Thomason Decl. ¶¶ 1-8.

Plaintiff Kathleen Raker ("Ms. Raker") is a 41-year-old woman whose mother and maternal grandmother died from breast cancer. She obtained *BRCA1/2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA1/2* genetic testing offered by Myriad that looks for other large DNA rearrangements that are not included in Myriad's standard full sequencing test, but informed her that it was unclear whether her insurance would cover the full cost of that test. Ms. Raker is unable to afford the extra cost. Raker Decl. ¶¶ 1-9.

Defendant USPTO is an agency of the Commerce Department of the United States with its principal office in Alexandria, Virginia. USPTO Answer ¶ 27.

Defendant Myriad is a for-profit corporation incorporated in Delaware with its principal place of business in Salt Lake City, Utah. Myriad is the former co-owner of several of the patents-in-suit and the current exclusive licensee of the patents-in-suit. Myriad is the sole provider of full sequencing of *BRCA1* and *BRCA2* genes in the United States on a commercial basis. Myriad Answer

¶ 28.

The University of Utah Research Foundation, whose directors are named as defendants in their official capacity, is an owner or part-owner of each of the patents-in-suit. Myriad Answer ¶ 29.

Amici curiae American Medical Association, American Society of Human Genetics, American College of Obstetricians and Gynecologists, American College of Embryology, and The Medical Society of the State of New York are non-profit organizations representing physicians and medical students throughout the United States, including New York; professionals in the field of human genetics, including researchers, clinicians, academicians, ethicists, genetic counselors and nurses whose work involve genetic testing; women's health care professionals; and embryologists. These amici contend that the patents-in-suit are directed to unpatentable natural phenomena in violation of Article I, Section 8, Clause 8 of the Constitution, and 35 U.S.C. § 101, are unnecessary to promote innovation in genetic research, and violate medical and scientific ethics.

Amici curiae March of Dimes Foundation, Canavan Foundation, Claire Altman Heine Foundation, Breast Cancer Coalition, Massachusetts Breast Cancer Coalition, National Organization for Rare Disorders, and National Tay-Sachs & Allied Diseases Association are non-profit organizations dedicated to advancing the treatment of a variety of genetic diseases, including breast cancer, Tay-Sachs, Spinal Muscular Dystrophy, Canavan disease, and other rare genetic disorders. These amici contend that Myriad's patents represent patents on natural phenomena and laws of nature, thereby restricting future research and scientific progress.

Amici curiae National Women's Health Network, Asian Communities for Reproductive Justice, Center for Genetics and Society, Generations Ahead, and Pro-Choice Alliance for Responsible Research are non-profit organizations seeking to improve the health of women; promote reproductive justice; encourage responsible use and governance of genetic, reproductive and biomedical technologies; promote policies on genetic technologies that protect human rights; promote accountability, safety, and social justice in biomedical research from a women's rights perspective. These amici contend that isolated DNA

constitutes an unpatentable product of nature whose patenting harms women by stifling innovation and interfering with patient access to medical testing and treatment. These amici also contend that human genes and the information contained therein constitute part of the common heritage of humanity, and patenting human gene sequences is contrary to both international law and treatises as well as the public trust doctrine.

Amici curiae The International Center for Technology Assessment, Indigenous People Council on Biocolonialism, Greenpeace, Inc., and Council for Responsible Genetics are non-profit organizations dedicated to assisting the public and policy makers in understanding how technology affects society, protecting the cultural heritage and genetic materials of indigenous peoples; addressing global environmental problems; and protecting the public interest and fostering public debate about the social, ethical, and environmental implications of genetic technologies. These amici contend that the patents-in-suit claim unpatentable products of nature and that gene patents have significant negative consequences, including privatization of genetic heritage in violation of fundamental precepts of common heritage, public domain, and

the public trust doctrine; creation of private rights of unknown scope and significance; facilitate the exploitation of indigenous peoples; and violation of patients' rights to informed consent.

Amicus curiae Biotechnology Industry Organization ("BIO") is the country's largest biotechnology trade association, representing over 1200 companies, academic institutions, and biotechnology centers in all 50 states. BIO members are involved in the research and development of biotechnological healthcare, agricultural, environmental, and industrial products. BIO member companies range from start-up businesses and university spin-offs to large Fortune 500 corporations. BIO contends that patents directed to isolated DNA fall within the categories of patent-eligible subject matter because they differ "in kind" from naturally-occurring DNA. The BIO also contends that patents such as the ones in dispute here provide incentives for investment in biotechnology that promotes the advancement of science.

Amicus curiae Boston Patent Law Association ("BPLA") is a non-profit association of attorneys and other intellectual property professionals. BPLA's members serve

a broad range of clients who rely on the patent system, including independent investors, corporations, investors, and non-profit and academic institutions, such as universities and research hospitals. BPLA contends that patents, including patents on gene-related inventions, promote innovation by protecting investments in the innovation process. It further contends that the patents-in-suit satisfy the requirements of 35 U.S.C. § 101 as well as the Constitution.

Amicus curiae Rosetta Genomics, Inc. is a wholly owned subsidiary of amicus curiae Rosetta Genomics, Ltd., a molecular diagnostics company that provides diagnostic tests for cancer and which owns several patents claiming isolated nucleic acid sequences. Amicus curiae George Mason University ("George Mason") is a public university located in Virginia. Research conducted at George Mason has been incorporated into patent applications covering cancer diagnostics. These amici contend that the question of patentability of human gene sequences is appropriately left to Congress; that the patents-in-suit promote, rather than hinder innovation; and that the challenged patents are lawful under 35 U.S.C. § 101 and the Constitution.

Amicus curiae BayBio is an independent, non-profit 501(c)(6) trade association serving the life sciences industry in Northern California, and represents more than 330 companies involved in the research and development of treatments, cures, and diagnostics. Amicus curiae Celera Corporation is a manufacturer of diagnostic products that include gene-based products used in genetic testing. Amicus curiae The Coalition for 21st Century Medicine represents some of the world's most innovative diagnostic technology companies, clinical laboratories, researchers, physicians, venture capitalists, and patient advocacy groups that share a common mission to develop advanced diagnostics that improve the quality of healthcare for patients. Amicus curiae Genomic Health, Inc., is a life sciences company committed to improving the quality of cancer treatment decisions through genomics-based clinical laboratory services and currently offers the Oncotype DX breast cancer assay, which predicts the likelihood of the recurrence of specific types of breast cancer and whether a patient will benefit from certain treatment strategies. Amicus curiae Qiagen, N.V. is a leading provider of innovative sample and assay technologies and products which are considered standard for use in molecular diagnostics, applied testing, and academic and pharmaceutical research

and development. Amicus curiae Target Discovery, Inc. discovers, validates, and utilizes protein isoforms to improve clinical diagnosis and management of disease. Amicus curiae XDx, Inc., is a molecular diagnostics company focused on the discovery, development and commercialization of non-invasive gene expression testing in the areas of transplant medicine and autoimmunity through the use of modern genomics and bioinformatics technology. These amici contend that patent exclusivity is required for the development of personalized medicine and that the challenged patents satisfy the requirements of 35 U.S.C. § 101 and the Constitution. In addition, the amici contend that the harm alleged by Plaintiffs can be redressed through traditional judicial remedies and do not require a finding that isolated DNA constitutes unpatentable subject matter.

Amicus curiae Kenneth Chahine, Ph.D. ("Professor Chahine"), is a Visiting Professor of Law at S.J. Quinney College of Law at the University of Utah. Professor Chahine contends that the scope of the claims-in-suit are sufficiently limited to avoid claiming products of nature and that the claims directed to isolated DNA and diagnostic process satisfy the requirements of patentable subject

matter under 35 U.S.C. § 101.

Amicus curiae Kevin E. Noonan, Ph.D. ("Dr. Noonan"), is a patent attorney with McDonnell Boehnen Hulbert & Berghoff LLP. Dr. Noonan contends that isolated human DNA constitutes patentable subject matter and that a ban on patenting isolated human DNA would negatively affect the development of human therapeutics, the development of personalized medicine, and the scientific research in general.

III. THE FACTS

The facts as set forth in this section are taken from the parties' respective statements and counterstatements pursuant to Local Civil Rule 56.1 and the affidavits submitted by the parties and amici and are not in dispute except where noted.

A. The Development of Genetics as a Field of Knowledge

The field of genetics - the science of heredity and variation in living organisms - and the concept of units of heredity that could be transmitted from one

generation to another originated in the 19th century from experiments with pea plants conducted by Gregor Mendel. Mendel showed that certain traits are passed on from parent to offspring as discrete entities and do not appear blended in the offspring. He hypothesized that it was the plant's genotype, or assortment of hereditary factors, that determined the plant's phenotype, or appearance. Mason Decl. ¶ 8. In 1909, this unit of inheritance was termed a "gene." Yet the gene remained an abstract concept until 1915, when it was shown that genes corresponded to physical spans of chromosomal material. Mason Decl. ¶ 9.

In 1944, scientists determined that the chemical compound known as deoxyribonucleic acid, or DNA,[3] served as the carrier for genetic information by demonstrating that DNA extracted from one strain of bacteria and transferred to another strain could transfer certain characteristics found in the first strain. Oswald Theodore Avery, et al., Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III, 79 J. Exp. Med. 137-

[3] Scientists had learned to extract DNA from the body by removing it from the rest of the cellular material since as early as 1869. Ralf Dahm, Discovering DNA: Friedrich Miescher and the Early Years of Nucleic Acid Research, 122 Human Genetics 565-581, 567-68 (2008).

158 (1944).

On April 25, 1953, James Watson and Francis Crick published their determination of the famous double-helix structure of DNA in the journal *Nature*. James D. Watson & Francis H.C. Crick, A Structure for Deoxyribose Nucleic Acid, 171 Nature 737-38 (1953). Dr. Crick subsequently contributed to the decryption of the genetic code and proposed "the central dogma" of molecular biology: (1) information is encoded in a segment of DNA, i.e., a gene; (2) transmitted through a molecule called RNA; and then (3) utilized to direct the creation of a protein, the building block of the body. Mason Decl. ¶ 10.

Our understanding of the DNA contained within our cells has since grown at an exponential rate and has included the landmark completion of the first full-length sequence of a human genome, containing 25,000 genes, as a result of the work performed by the Human Genome Project from 1990 to 2003. Sulston Decl. ¶¶ 11, 22. Access to the information encoded in our DNA has presented expansive new possibilities for future biomedical research and the development of novel diagnostic and therapeutic approaches. How this genomic information is best harnessed for the

greater good presents difficult questions touching upon innovation policy, social policy, medical ethics, economic policy, and the ownership of what some view as our common heritage.

B. Molecular Biology and Gene Sequencing

An understanding of the basics of molecular biology is required to resolve the issues presented and to provide the requisite insight into the fundamentals of the genome, that is, the nature which is at the heard of the dispute between the parties. What follows represents the standard undisputed knowledge of those in the field of molecular biology as set forth in the parties' 56.1 Statements and expert declarations. Citations are also made to two established texts in the field: Bruce Alberts, et al., *Molecular Biology of the Cell* (4th ed. 2002) ("*The Cell*") and James Watson, et al., *Molecular Biology of the Gene* (6th ed. 2008) ("*The Gene*").

1. DNA

DNA is a chemical molecule composed of repeating chemical units known as "nucleotides" or "bases." DNA is

composed of four standard nucleotides: adenine, thymine, cytosine, and guanine. As shorthand, scientists denote nucleotides by the first letter of the names of their bases: "A" for adenine; "G" for guanine; "T" for thymine; and "C" for cytosine. These nucleotide units are composed of several chemical elements, namely carbon, hydrogen, oxygen, nitrogen, and phosphorus, and are linked together by chemical bonds to form a strand, or polymer, of the DNA molecule. Kay Decl. ¶¶ 14, 125; Linck Decl. ¶ 70. Although it can exist as a single strand of nucleotides, DNA typically exists as a "double helix"[4] consisting of two intertwined strands of DNA that are chemically bound to each other. This structure is possible because of a property of DNA known as "base pair complementarity" or "base pairing," in which adenine on one strand of DNA always binds to thymine on the other strand of DNA, and guanine on one strand always bind to cytosine on the other strand. Kay Decl. ¶ 129. For example, if a portion of one strand of DNA has the nucleotide sequence ACTCGT, the corresponding section of DNA on the complementary strand will have the nucleotide sequence TGAGCA.

[4] It was the description of this famous "double-helix" structure that earned Watson and Crick the Nobel Prize.

Genes are basic units of heredity found in all living organisms and are responsible for the inheritance of a discrete trait. Sulston Decl. ¶ 11. In molecular terms, a gene is composed of several, typically contiguous, segments of DNA. Kay Decl. ¶ 142. Each gene is typically thousands of nucleotides long and usually "encodes" one or more proteins, meaning it contains the information used by the body to produce those proteins. Some of the segments of DNA within a gene, known as "exons" or "coding sequences," contain sequences necessary for the creation of a protein, while other segments of DNA, known as "introns," are not necessary for the creation of a protein.[5] See Mason Decl. ¶ 11; Kay Decl. ¶ 151; Schlessinger Decl. ¶ 14. DNA encodes proteins by way of three nucleotide combinations, termed "codons," that correspond to one of twenty amino acids that constitute the building blocks of proteins. Sulston Decl. ¶¶ 14-15. For example, the codon adenine-thymine-guanine (ATG) encodes the amino acid methionine. Kay Decl. ¶ 158. However, because there are only twenty different amino acids but 64 possible codons that can be derived from combinations of the four DNA nucleotides, most amino acids are encoded by more than one DNA codon. *The*

[5] Introns can contain regulatory sequences that affect the body's rate of production of the protein encoded by a gene. Kay Decl. ¶ 151.

Gene at 37 & Table 2-3.

Together, the approximately 25,000 genes in the human body make up the human genome.[6] The genome, and the genes within it, are contained within almost every cell in the human body and define physical traits such as skin tone, eye color, and sex, in addition to influencing the development of conditions such as obesity, diabetes, Alzheimer's disease, and bipolar disorder. Mason Decl. ¶¶ 4-5; Sulston Decl. ¶¶ 10-11.

The linear order of DNA nucleotides that make up a polynucleotide, such as a gene, is referred to as the "nucleotide sequence," "DNA sequence," or "gene sequence."[7] Kay Decl. ¶ 126; Schlessinger Decl. ¶ 19; Linck Decl. ¶ 45; Sulston Decl. ¶ 16; Mason Decl. ¶ 13; Chung Decl. ¶ 10. Gene sequences constitute biological information insofar as they describe the structural and chemical properties of a particular DNA molecule and serve as the cellular "blueprint" for the production of proteins. Sulston Decl. ¶ 16; Kay Decl. ¶ 126; Schlessinger Decl. ¶ 19; Linck Decl.

[6] Genome is defined as "[t]he totality of genetic information belonging to a cell or an organism; in particular, the DNA that carries this information." *The Cell* at G:15.
[7] By analogy, if a gene is the equivalent of a word, then the nucleotide sequence is the equivalent of the word's spelling.

¶¶ 45, 46. Genes and the information represented by human gene sequences are products of nature universally present in each individual, and the information content of a human gene sequence is fixed. While many inventive steps may be necessary to allow scientists to extract and read a gene sequence, it is undisputed that the ordering of the nucleotides is determined by nature. Sulston Decl. ¶ 10, 17; Ostrer Decl. ¶ 14; Chung Decl. ¶ 25; Ledbetter Decl. ¶ 27; Leonard Decl. ¶ 15.

Scientists often use the term "wild-type" to refer to the "normal" human gene sequence, i.e. the sequence of a gene without any variations,[8] against which individuals' gene sequences are compared. Mason Decl. ¶ 17; Grody Decl. ¶ 46. Variations in the human genome are very common: aside from identical twins, the genomes of any two individuals are estimated to have one to five nucleotide differences for every 1000 nucleotides. Mason Decl. ¶ 14; Sulston Decl. ¶ 12.

Variations in the human genome, also known as

[8] At the same time there is an increasing recognition that the notion of a single "normal" gene sequence may not be entirely accurate in light of the high frequency of variations in a gene's sequence between individuals. Mason Decl. ¶ 17. For purposes of this opinion, however, genes are treated as having a single "normal" DNA sequence.

"mutations," can occur at different scales. Small scale variations can be manifested as slight sequence differences between the same genes in different individuals. Thus, for example, if the wild-type sequence of a portion of a gene is represented by GACTCG, a variation of that sequence might omit the first C (resulting in GATCG) or contain an extra C at that point (resulting in GACCTCG) or reverse the order of two of the letters (e.g., GCATCG). Mason Decl. ¶ 16. Alternatively, there can be large scale variations, such as the addition or deletion of substantial chromosomal regions. Thus, a particular gene may omit several hundred letters at one point or may add several hundred letters where they do not normally exist in the wild-type gene sequence. Even larger variations, known as structural variants, also can occur, involving the deletion or duplication of up to millions of nucleotides. Extra copies or missing copies of the genome that are larger than 1000 nucleotides are called "copy number variants" ("CNVs"). Mason Decl. ¶ 15, 18.

Some of these mutations have little or no effect on the body's processes, while other mutations, including those that appear to correlate with an increased risk of particular diseases, do interfere with the body's

processes.[9] There are also variants of uncertain significance ("VUS"): variants whose effect on the body's processes, if any, is currently unknown. Mason Decl. ¶ 19; Sulston Decl. ¶ 18; Kay Decl. ¶ 76.

DNA as it is found in the human body – "native DNA" or "genomic DNA" – is packaged, along with proteins, into complex structures known as chromosomes, which contain the vast majority of the genes located in the cells of the human body. Kay Decl. ¶ 131; Schlessinger Decl. ¶ 12. This mixture of DNA and proteins that makes up chromosomes is also referred to as chromatin. See *The Gene* at 135. Genes are organized on forty-six chromosomes (twenty-three of which are inherited from the mother, and twenty-three of which are inherited from the father) which together constitute the vast majority of the human genome.[10] Mason Decl. ¶ 5. The proteins within the chromosomes are bound[11]

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[9] The correlation between a particular mutation and disease susceptibility is not self-evident from the mutation itself; rather, extensive statistical analysis is required to identify which alterations in the nucleotide sequence correlate with a particular medical condition, a process which may take many years. Kay Decl. ¶ 190.

[10] A very small fraction of human genes are located in a cellular organelle known as the mitochondria. Kay Decl. ¶ 144; Schlessinger Decl. ¶ 23. Neither party appears to believe that a discussion of mitochondrial DNA bears much relevance to the legal issues presented.

[11] The ionic chemical bonds that exists between proteins and DNA molecules differ from the covalent chemical bonds which hold DNA itself together. See *The Cell* at 198 (describing DNA in the cell as "associated with proteins that fold and pack the fine DNA thread into a more compact structure."); id. at 208 Fig. 4-24 (demonstrating

to the DNA molecules and modulate the structure and function of the DNA molecules to which they are associated. Kay Decl. ¶ 131; Schlessinger Decl. ¶ 12; *The Cell* at 198, 208, Fig. 4-24. This interaction between chromosomal proteins and native DNA is one method by which the body establishes which genes are inactive, which genes are active, and the level of activity. Kay Decl. ¶ 132. Some DNA in the body also undergoes chemical modifications, such as methylation,[12] which can affect the level of activity of a gene, but does not affect the nucleotide sequence of the gene. Kay Decl. ¶ 132; Mason Supp. Decl. ¶ 22.

2. Extracted and purified DNA

Native DNA may be extracted from its cellular environment, including the associated chromosomal proteins, using any number of well-established laboratory techniques. Grody Decl. ¶ 13; Leonard Decl. ¶ 33. A particular segment of DNA, such as a gene, contained in the extracted DNA may then be excised from the genomic DNA in which it is embedded to obtain the purified DNA of interest. Kay Decl.

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dissociation of histone proteins from DNA by high salt solution, indicating lack of covalent bond between DNA and histones).

[12] Methylation refers to the addition of a small chemical group composed of one carbon atom and three hydrogen atoms (CH_3), known as a "methyl group," to the nucleotides of a segment of DNA. See *The Cell* at 430.

¶¶ 133, 137. DNA molecules may also be chemically synthesized in the laboratory. Kay Decl. ¶¶ 17, 133, 137.

Although the parties use the term "isolated DNA" to describe DNA that is separated from proteins and other DNA sequences, the term "isolated DNA" possesses a specific legal definition reflecting its use in the patents-in-suit. To avoid any confusion for purposes of this fact recitation, the term "extracted DNA" will be used to refer to DNA that has been removed from the cell and separated from other non-DNA materials in the cell (e.g., proteins); "purified DNA" will be used to refer to extracted DNA which has been further processed to separate the particular segment of DNA of interest from the other DNA in the genome; and "synthesized DNA" will be used to refer to DNA which has been synthesized in the laboratory.

As noted above, native DNA, unlike purified or synthesized DNA, is not typically found floating freely in cells of the body, but is packaged into chromosomes. Kay Decl. ¶¶ 131, 148. However, when DNA is copied, or replicated, in preparation for cell division, short segments of DNA are dissociated from the chromosomal proteins, although they are still contained within the

cell. Similarly, when a particular portion of DNA is transcribed into RNA, segments of DNA exist dissociated from the proteins normally bound to it. Mason Supp. Decl. ¶ 23.

Purified or synthesized DNA may be used as tools for biotechnological applications for which native DNA cannot be used. Kay Decl. ¶¶ 134, 138; Schlessinger Decl. ¶ 27. For example, unlike native DNA, purified or synthesized DNA may be used as a "probe,"[13] which is a diagnostic tool that a molecular biologist uses to target and bind to a particular segment of DNA, thus allowing the target DNA sequence to be detectable using standard laboratory machinery. Kay Decl. ¶ 135; Schlessinger Decl. ¶ 29. Purified or synthesized DNA can also be used as a "primer"[14] to sequence a target DNA, a process used by molecular biologists to determine the order of nucleotides in a DNA molecule, or to perform polymerase chain reaction ("PCR") amplification, a process which utilizes target-DNA specific primers to duplicate the quantity of target DNA exponentially. Critchfield Decl. ¶ 40; Kay Decl. ¶ 184.

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[13] A probe is a DNA fragment that is usually between 100-1000 nucleotides long. Kay Decl. ¶ 135.

[14] A primer is a DNA fragment, usually between 15 and 30 nucleotides long, that binds specifically to a target DNA sequence. Kay Decl. ¶ 183.

During this process, the DNA molecule being used as a probe or a primer binds, or "hybridizes," to a specific nucleotide sequence of a DNA target molecule, such as the *BRCA1* or *BRCA2* gene. This sequence-specific binding of two strands of DNA results from the same base-pairing phenomenon which allows two complementary strands of DNA to form the double helix structure. As a result, a strand of isolated DNA being used as a primer with the sequence ATGTCG, for example, will bind specifically to the portion of the target DNA molecule containing the nucleotide sequence TACAGC. The hybridization of a primer or probe to a DNA target, such as *BRCA1* or *BRCA2*, results in the formation of a "hybridization product" that either acts as a substrate for the enzymes used in the sequencing or amplification reaction or permits the detection of the target DNA. See Kay Decl. ¶¶ 138, 183; Schlessinger Decl. ¶ 30; *The Gene* at 105-06; 113-15.

The utility of purified *BRCA1/2* DNA molecules as biotechnological tools therefore relies on their ability to selectively bind to native or isolated *BRCA1/2* DNA molecules, which ability is a function of the isolated DNA's nucleotide sequence. Kay Decl. ¶ 138.

3. RNA

Ribonucleic acid ("RNA") is another nucleic acid found in cells. Like DNA, an RNA molecule is composed of a combination of four different nucleotides, three of which are the same bases incorporated into DNA: adenine, cytosine, and guanine. Unlike DNA, however, RNA utilizes uracil as the fourth nucleotide base, rather than thymine. In addition, the sugar-phosphate backbone in RNA is chemically different from the sugar-phosphate backbone of DNA. Kay Decl. ¶ 170.

The creation of proteins, which do the work of the body, comprises two steps: transcription and translation. Transcription is the process by which a temporary copy of a particular DNA sequence, in the form of an RNA molecule, is generated. Mason Decl. ¶¶ 11-12; Kay Decl. ¶¶ 149, 150. During transcription, a discrete segment of DNA unwinds itself inside the cell and the bases of the DNA molecule act as "clamps" that hold the bases of the newly forming RNA molecule in place while the chemical bonds of its sugar-phosphate backbone are formed. Kay Decl. ¶ 150. Each nucleotide in the DNA strand corresponds

to a nucleotide to be incorporated into the newly forming RNA molecule: adenine on the DNA molecule binds to and thereby acts as a clamp for RNA nucleotide uracil, thymine for adenine, guanine for cytosine, and cytosine for guanine. Kay Decl. ¶ 150. This newly generated RNA is termed "pre-messenger RNA" or "pre-mRNA" and, like the DNA from which it was generated, contains both introns and exons. In a process known as "splicing," the introns are physically cut out of the pre-mRNA by the cell and the remaining RNA segments containing the exons are rejoined, or "ligated," together in consecutive order to form the final "messenger RNA," or "mRNA." Mason Decl. ¶ 11; Kay Decl. ¶ 151; Schlessinger Decl. ¶ 14. Pre-mRNAs can also undergo a process known as "alternative splicing," in which different combinations of exons from the same pre-mRNA molecule are ligated together to yield different final mRNA products.[15] Kay Decl. ¶ 152; Schlessinger Decl. ¶ 14.

During translation, an mRNA molecule serves as a template for the assembly of a protein. Kay Decl. ¶ 157.

[15] For example, a pre-mRNA molecule containing exons ("E") numbered 1-6, with introns ("I") between each exon whose structure is represented as follows: E1+I1+E2+I2+E3+I3+E4+I4+E5+I5+E6. After splicing, the introns would be removed to form an mRNA composed only of exons: E1+E2+E3+E4+E5+E6. On the other hand, the same pre-mRNA molecule might undergo alternative splicing to form final mRNAs with a variety of different exon compositions: for example, E1+E2+E5; E1+E3+E6; and E1+E4+E6.

In a process that parallels the transcription of DNA, the mRNA bases, along with other proteins in the cell, serve as clamps to hold the corresponding amino acids in place while the chemical bonds between the individual amino acids are formed. Kay Decl. ¶ 157. The three-nucleotide codons originally found in DNA and copied into mRNA determine which amino acids are incorporated into the protein and the order in which they are incorporated. Kay Decl. ¶ 157.

4. cDNA

Complementary DNA, or "cDNA," is a type of DNA molecule generated from mRNA during a process known as "reverse transcription" which is catalyzed by a protein known as "reverse transcriptase." cDNA derives its name from the fact that it is "complementary" to the mRNA from which it is produced - that is, each base in the cDNA can bind to the corresponding base in the mRNA from which it is generated. Kay Decl. ¶ 161. Because it is derived from mRNA, a cDNA molecule represents an exact copy of one of the protein coding sequences encoded by the original genomic DNA. Leonard Decl. ¶ 75. In this respect, cDNA contains the identical protein coding informational content as the DNA in the body, even though differences exist in

its physical form. Mason Decl. ¶ 32.

During reverse transcription, each base of the mRNA serves as a clamp for its complementary nucleotide to be incorporated into the new cDNA molecule while the chemical bonds between the nucleotides of the cDNA strand are formed. Much like transcription, uracil on the mRNA binds to and thereby acts as a clamp for the nucleotide adenine, adenine for thymine, guanine for cytosine, and cytosine for guanine. Kay Decl. ¶ 165. The synthesis of cDNA from very long mRNA molecules, such as *BRCA1* and *BRCA2*, often does not result in a cDNA strand that is as long as the mRNA chain. Kay Decl. ¶ 166.

cDNA is typically generated by scientists in a laboratory. Kay Decl. ¶ 164, Linck Decl. ¶ 48. However, naturally occurring cDNAs, known as "pseudogenes," exist in the human genome and are structurally, functionally, and chemically identical to cDNAs made in the laboratory. Mason Supp. Decl. ¶¶ 18-21; Nussbaum Decl. ¶¶ 41-42.

cDNA possesses certain structural and functional differences from native DNA. In contrast to most forms of native DNA, cDNA does not contain non-coding intronic

sequences because it is derived from mRNA in which the introns have been removed. As a result, the production of proteins from cDNA does not require RNA splicing, in contrast to the production of proteins from native DNA as described above. Some cDNAs cannot be used to produce proteins without the addition of certain regulatory sequences, although other cDNAs possess some of the necessary regulatory sequences. cDNAs also usually contain nucleotides corresponding to the so-called "poly A tail" sequence found in mRNA, which native DNA does not possess. In addition, as mentioned above, native DNA is often (although not always) chemically modified in the body, e.g., by methylation, while cDNA generated in the laboratory is not so modified. Kay Decl. ¶¶ 168, 169; Mason Supp. Decl. ¶¶ 18-22; Nussbaum Decl. ¶¶ 41-42. cDNA also differs from mRNA in that it is a more stable compound and requires both transcription and translation to produce protein, rather than simply translation, as is the case with mRNA. Kay Decl. ¶ 171.

Much like purified DNA, cDNA can be used as a tool for biotechnological and diagnostic applications for which native DNA cannot be used. Kay Decl. ¶ 162. In addition, a scientist seeking to learn more about a protein

of interest may transfer a cDNA encoding the protein into a recipient cell that does not normally express that protein. If the cDNA is operatively linked to particular "promoter" sequences that initiate transcription from the cDNA, the recipient cell will then express the protein of interest. Kay Decl. ¶ 163.

5. DNA sequencing

DNA sequencing is the process by which one "reads," or determines the ordering of the nucleotides within a DNA molecule. Sulston Decl. ¶ 20; Kay Decl. ¶ 138. In the context of a gene or a portion of the genome, sequencing is designed to illuminate the information that nature has dictated in that person's genome, and the sequencing process, by design, does not alter the information content of the native DNA sequence. Sulston Decl. ¶ 27; Mason Decl. ¶ 32. In that respect, sequencing is analogous to examining something through a microscope insofar as it makes visible something that exists in nature but is too small to be seen otherwise. Mason Decl. ¶ 23. Gene sequencing is used in diagnostic testing, such as Myriad's tests, to determine whether a gene contains mutations that have been associated with a particular

condition. Sulston Decl. ¶ 24; Chung Decl. ¶ 10; Swisher Decl. ¶¶ 23-26; Mason Decl. ¶ 21. These mutations, along with any association with a propensity to develop a particular disease, are caused by nature. Chung Decl. ¶ 10; Mason Decl. ¶ 20; Sulston Decl. ¶¶ 19, 27; Ledbetter Decl. ¶ 26. Therefore, the significance of any person's gene sequence, including its relationship to any disease, is dictated by nature. Mason Decl. ¶ 32.

Sequencing is often used to identify single nucleotide substitutions or the insertion or deletion of a small number of nucleotides in a gene. Swisher Decl. ¶ 23; Kay Decl. ¶ 180. However, even full sequencing of an entire gene can miss large genomic rearrangements in which whole sections of the gene have been deleted or moved to a different part of the genome. Other tests have been developed that better detect these large rearrangements. Swisher Decl. ¶ 24; Ledbetter Decl. ¶¶ 16-17.

Sequencing native DNA first requires that cells of a tissue sample[16] be broken open to permit extraction of the DNA contained within the cells. Sulston Decl. ¶ 25.

[16] Various types of patient samples can be used, e.g., blood, tumor tissue, or non-tumor tissue. Kay Decl. ¶ 186.

The extracted DNA of the entire genome contains over three billion nucleotides, of which the gene of interest comprises a very small portion. Kay Decl. ¶ 178. *BRCA1/2* sequencing by Myriad follows the typical process for sequencing extracted genomic DNA, which begins with obtaining a sufficient quantity of the *BRCA1/2* genomic DNA to permit its sequencing. Critchfield Decl. ¶ 40.

Under the current state of the art, the only practical way to obtain a sufficient amount of *BRCA1/2* genomic DNA for mutation detection purposes is to PCR amplify the genomic DNA in segments. Critchfield Decl. ¶ 40. In order to design the necessary primers to PCR amplify the correct region of the genome, at least a portion of the sequence of the target DNA molecule must be known. Kay Decl. ¶ 184. Typically, each exon of the *BRCA1/2* genes, including a small adjacent portion of the flanking introns, is separately amplified by PCR into one or more amplified DNA fragments, also called "amplicons." The *BRCA1* and *BRCA2* genes have a total of 48 coding exons containing over 15,700 nucleotide base pairs. More than 50 amplicons are typically produced as part of Myriad's *BRCA1/2* testing. Critchfield Decl. ¶ 40.

Following PCR amplification of the target DNA, a sequencing reaction is performed to determine the nucleotide sequence of the amplicon. Kay Decl. ¶ 183. As with PCR, at least some of the target sequence must be known in order to design a primer specific to the target DNA to be sequenced. Kay Decl. ¶¶ 177, 179, 183. For this reason, primers that bind only to specific DNA sequences in the *BRCA1* and *BRCA2* genes permit the analysis of a patient's native DNA sequence to determine if the nucleotide composition is the same or different from the nucleotide composition of the normal *BRCA1* and *BRCA2* gene. Kay Decl. ¶ 187. Gene sequencing also sometimes utilizes cDNA as the DNA template. Leonard Decl. ¶ 75.

The techniques required for gene sequencing are well-known and understood by scientists skilled in molecular biology, and scientists and clinicians sequence and analyze genes literally every day. Chung Decl. ¶¶ 10-11; Mason Decl. ¶ 22; Hegde Decl. ¶¶ 6-7. However, because sequencing requires knowledge of the sequence of a portion of the target sequence, some ingenuity and effort is required for the initial sequencing of a target DNA. See Kay Decl. ¶ 183; Klein Decl. ¶ 32-34.

C. The Development of the Patents-in-Suit

Breast cancer is the most frequently diagnosed cancer worldwide and is the leading cause of cancer death for women in Britain and the second leading cause of cancer death for women in the United States. Parthasarathy Decl. ¶ 8.[17] Ovarian cancer is the eighth most common cancer in women and causes more deaths in the Western world than any other gynecologic cancer. Swisher Decl. ¶ 10.

Throughout the 1980s, organizations dedicated to breast cancer awareness began efforts to increase public and governmental awareness of the breast cancer epidemic. In 1991, the U.S. Department of Defense created a research program devoted to breast cancer research. Over the years this funding has grown from less than $90 million during the fiscal year 1990 to more than $2.1 billion during the fiscal year 2008. Parthasarathy Decl. ¶ 10.

Throughout the 1980s, scientists from the United States, England, France, Germany, Japan, and other

[17] Dr. Parthasarathy has researched the development of genetic testing for breast and ovarian cancer in the United States and Britain and has interviewed over 100 individuals involved in the process, including research scientists, officials at research institutions, health care professionals, patent office officials, bioethicists, and journalists. Parthasarathy Decl. ¶ 6.

countries sought to be the first to identify DNA nucleotide sequences associated with breast cancer. Parthasarathy Decl. ¶ 11. In 1989, various European and American research laboratories participated in the International Breast Cancer Linkage Consortium (the "Consortium"), and in 1990, a group of researchers led by Mary-Claire King ("Dr. King") at the University of California, Berkeley, published a landmark paper demonstrating for the first time that a gene linked to breast cancer, whose sequence was unknown but which was later designated Breast Cancer Susceptibility Gene 1 (*BRCA1*), was located on a region of chromosome 17. See Jeff M. Hall, et al., Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21, 250 Science 1684-89 (1990); Parthasarathy Decl. ¶ 11. Soon afterwards, research intensified as teams around the world, including groups led by Dr. King, Dr. Mark Skolnick ("Dr. Skolnick") (co-founder of Myriad), and Dr. Michael Stratton ("Dr. Stratton") (Institute for Cancer Research, London ("ICR")), focused in on this region of the genome in an attempt to be the first to determine the DNA sequence of *BRCA1*. Parthasarathy Decl. ¶ 11.

Dr. Skolnick, a 1968 economics graduate of the University of California, Berkeley, had become interested

in the application of demography to the study of genetics while doing research for his Ph.D. in genetics, which he received from Stanford University in 1975. While reconstructing genealogies in Italy, he met three Mormons who were microfi1ming parish records and from whom he learned of the resources of the Utah Genealogical Society in Salt Lake City. Thereafter, in 1973, after an inquiry from the organizers of a cancer center at the University of Utah, Dr. Skolnick suggested linking the Utah Mormon Genealogy with the Utah Cancer Registry. To further this effort, a familial cancer screening clinic was established and a program for mapping genes was developed. Skolnick Decl. ¶¶ 7, 11, 12.

Following publication of the King group's study relating to *BRCA1* in the fall of 1990, Dr. Skolnick and his collaborators concluded that additional resources would be required to compete with the team of Dr. Francis Collins, which had received a substantial grant from the National Institutes of Health ("NIH"), Skolnick Decl. ¶¶ 13, 14, and in 1991 Myriad was founded by Dr. Skolnick and a local venture capital group interested in genetics. Myriad received $5 million in funding in 1992, $8 million in 1993, and $9 million in 1994. Skolnick Decl. ¶ 16.

Locating the *BRCA1* gene relied on the use of linkage analysis, in which correlations between the occurrence of cancer and the inheritance of certain DNA markers among family members were used to identify, or "map," the physical location of, the *BRCA1* gene within the human genome. See '282 patent, col. 7:39-52. Once the physical location had been narrowed down to a sufficiently small region of the genome, Myriad was able to directly analyze the sequence of the DNA in this region and identify the nucleotides comprising the *BRCA1* gene. See '282 patent, col. 7:53-8:7. Successful linkage analysis requires large and genetically informative families, or kindreds, and detailed family information, such as detailed genealogical records, are an important component to this analysis. Shattuck Decl. ¶¶ 10, 13; '282 patent, col. 8:16-29.

In September 1994, the group at Myriad, along with researchers from the National Institute for Environmental Health Sciences ("NIEHS") (a subdivision of the NIH), the University of Utah, McGill University, and Eli Lilly and Company announced that they had sequenced the *BRCA1* gene. See Yoshio Miki, et al., A Strong Candidate

for the Breast and Ovarian Cancer Susceptibility Gene *BRCA1*, 266 Science 66-71 (1994). In addition to funding the six NIEHS researchers who participated in the identification of *BRCA1*, the NIH had also provided approximately $2 million in funding to the University of Utah.[18] See id. at 71 n.52; Parthasarathy Decl. ¶ 18. According to one analysis, the NIH contributed one-third of the funding for the identification of *BRCA1*. Parthasarathy Decl. ¶ 18.

A dispute subsequently arose between Myriad and the NIH over the NIEHS scientists' exclusion as co-inventors on the *BRCA1* patents. Parthasarathy Decl. ¶ 19. The NIH maintained that its scientists had conducted some of the most important work leading up to the sequencing of the gene, including identifying the sequences of two of the *BRCA1* gene fragments and assembling the complete *BRCA1* sequence. Id. Myriad agreed to include the names of the NIEHS researchers as inventors on its patent application and pay inventors' royalties, although no payments appear to have been made as of 2005. Id.

[18] According to the description of author associations, the first and second authors of the paper were associated with the University of Utah.

Following the isolation of *BRCA1*, scientists continued to search for a second gene also believed to be linked with breast and ovarian cancer.[19] Parthasarathy Decl. ¶ 12. Myriad collaborated with several research groups, including scientists at the University of Laval in Quebec, Canada, the Hospital for Sick Children in Toronto, Canada, and the University of Pennsylvania in their search for this second gene. It also collaborated with a team of researchers led by Dr. Stratton at the ICR which, in November 1995, identified a mutation in breast cancer patients that appeared to be located in the as-yet unpublished *BRCA2* gene. Dr. Stratton ended the collaboration with Myriad upon learning of Myriad's plans to patent the *BRCA2* gene sequence. Sulston Decl. ¶ 30.

On December 21, 1995, Myriad filed for patents on the *BRCA2* gene in both the U.S. and Europe. Tavtigian Decl. ¶ 5. The next day, the Stratton group published its identification of the *BRCA2* gene in the journal *Nature*, and Myriad submitted the sequence of *BRCA2* to GenBank, an international depository of gene sequence information. Parthasarathy Decl. ¶ 12; Tavtigian Decl. ¶ 9; Richard

[19] The same positional cloning approach utilized to isolate the *BRCA1* gene was relied on to isolate the *BRCA2* gene. Tavtigian Decl. ¶ 4.

Wooster, et al., Identification of the Breast Cancer Susceptibility Gene *BRCA2*, 378 Nature 789-92 (1995). Subsequent analysis of the *BRCA2* sequence from the Stratton group indicated that while they had correctly sequenced the primary portion of the *BRCA2* gene, their published sequence had errors in both ends of the *BRCA2* gene. Tavtigian Decl. ¶¶ 7-10. Nonetheless, the consensus among the scientific community is that the Stratton group, rather than Myriad, was the first to sequence the *BRCA2* gene. Parthasarathy Decl. ¶ 13.

The isolation of the *BRCA1/2* genes required considerable effort on the part of Myriad and its collaborators as well as ingenuity in overcoming technical obstacles associated with the isolation process. However, the process and techniques used were well understood, widely used, and fairly uniform insofar as any scientist engaged in the search for a gene would likely have utilized a similar approach. Parthasarathy Decl. ¶ 19; Tavtigian Decl. ¶ 13.

D. Application of the Patents-in-Suit

Mutations in the *BRCA1/2* genes correlate with an

increased risk of breast and ovarian cancer. Women with *BRCA1* and *BRCA2* mutations face up to an 85% cumulative risk of breast cancer, as well as up to a 50% cumulative risk of ovarian cancer. Love Decl. ¶ 10; Parthasarathy Decl. ¶ 9. In addition, among the 10-15% of ovarian cancer cases that are inherited genetically, 80% of women diagnosed under the age of 50 carry mutations in their *BRCA1* genes and 20% carry mutations in their *BRCA2* genes. The women with inherited *BRCA1* mutations have a 40-52% cumulative risk of ovarian cancer by the time they reach 70 years old. For women with inherited *BRCA2* mutations, the risk is approximately 15-25%. Swisher Decl. ¶ 11. Male carriers of mutations are also at an increased risk for breast and prostate cancer. Love Decl. ¶ 10.

The existence of *BRCA1/2* mutations is therefore an important consideration in the provision of clinical care for breast and/or ovarian cancer. A patient will not only learn of her risk for hereditary breast and ovarian cancer, but also can gain information that may be useful in determining prevention and treatment options. This information is useful for women who are facing difficult decisions regarding whether or not to undergo prophylactic surgery, hormonal therapy, chemotherapy, and other

measures. Swisher Decl. ¶ 12; Love Decl. ¶ 11. Testing results for the *BRCA1/2* genes can be an important factor in structuring an appropriate course of cancer treatment, since certain forms of chemotherapy can be more effective in treating cancers related to *BRCA1/2* mutations. Swisher Decl. ¶ 13; Love Decl. ¶ 18.

1. Myriad's *BRCA1/2* testing

Myriad offers multiple forms of *BRCA1/2* testing to the general public. Its standard test, called Comprehensive BRACAnalysis, originally only consisted of the full sequencing of the *BRCA1/2* genes. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 49. In 2002, Myriad supplemented its full sequencing analysis with a large rearrangement panel ("LRP") for detecting five common large rearrangement mutations which is now included in the Comprehensive BRACAnalysis. Critchfield Decl. ¶¶ 49, 51. In 2006, Myriad began offering a supplemental test to Comprehensive BRACAnalysis called the BRACAnalysis Rearrangement Test ("BART"), which, according to Myriad, can detect virtually all large rearrangement mutations in the *BRCA1* and *BRCA2*

genes.[20] Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 51.

2. Funding for Myriad's *BRCA1/2* tests

The Myriad tests are available to clinicians and patients at a cost of over $3000 per test. In 2008, the total cost to Myriad of providing these tests was $32 million with resulting revenues of $222 million. See Myriad Genetics, Inc., Annual Report (Form 10-K), at 27 (Aug. 28, 2008). In Ontario, where the regional public healthcare plan is ignoring Myriad's patent, the testing for breast cancer is performed for a third of Myriad's cost. See CBC News, Ontario to Offer New Genetic Test for Breast, Ovarian Cancer (Jan. 8, 2003), available at http://www.cbc.ca/health/story/2003/01/06/test_genetic030106.html.

Plaintiffs have noted several instances where women have been unable to obtain funding for all of Myriad's testing services. For example, Myriad refused to process Ms. Ceriani's sample because it did not accept

[20] Myriad also offers other more limited forms of *BRCA1/2* genetic testing. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26

coverage by Ms. Ceriani's insurance carrier. Unable to pay for Myriad's tests, and unable to find scholarship programs to fund her testing, Ms. Ceriani has not been tested. Ceriani Decl. ¶¶ 5-7. Ms. Fortune's insurance carrier is not accepted by Myriad, and Ms. Fortune is also unable to pay the full out-of-pocket cost of Myriad's test. Fortune Decl. ¶ 5.

Myriad's BART test is not covered by a number of insurers, and unless a patient is one of a limited number of "high risk patients" who meet certain clinical criteria established by Myriad, a patient must pay an extra fee for BART testing. Swisher Decl. ¶¶ 29-30; Reich Decl. ¶ 10; Parthasarathy Decl. ¶ 26; Critchfield Decl. ¶ 52. As a result of the cost of BART testing, the test is unavailable to women who would otherwise choose to utilize the test. Swisher Decl. ¶¶ 30-31; Reich Decl. ¶ 10. For example, Ms. Raker is unable to afford the extra cost for BART testing and has not been tested for large genomic rearrangements, despite the advice of her genetic counselor. Raker Decl. ¶¶ 7-11. Similarly, Ms. Thomason has been unable afford the BART testing recommended by her genetic counselor. Thomason Decl. ¶¶ 6-9.

Myriad has pursued Medicaid coverage for years, but has been unable to secure "participating provider" status in 25 states which would allow it to offer testing to that state's Medicaid patients. Myriad also has a financial assistance program which provides free testing to low-income and uninsured patients who meet certain economic and clinical requirements. In addition, Myriad provides free testing to independent non-profit institutions. In particular, Ms. Ceriani may be eligible to receive BRACAnalysis testing at no charge through the non-profit organization Cancer Resource Foundation, for which Myriad has provided free testing since 2009. Rusconi Decl. ¶¶ 4-6; Critchfield Decl. ¶ 33; Ogaard Decl. ¶¶ 4-6. Currently, 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield Decl. ¶¶ 32, 33, 52, 53.

A number of researchers, clinicians, and molecular pathologists have the personnel, equipment, and expertise to sequence and analyze genes, including the *BRCA1* and *BRCA2* genes, at a lower cost than Myriad's testing. Kazazian Decl. ¶¶ 8, 11; Matloff Decl. ¶ 12; Ostrer Decl. ¶¶ 8-9; Ledbetter Decl. ¶¶ 16-18. For example, the *BRCA1/2* testing previously conducted by the

Yale DNA Diagnostics Laboratory and the University of Pennsylvania Genetic Diagnostic Laboratory ("GDL") cost less than what Myriad charges, and testing by OncorMed, a one-time competitor, was cheaper than Myriad's testing. Matloff Decl. ¶ 7; Kazazian Decl. ¶ 8; Parthasarathy Decl. ¶ 24. However, on a "cost per exon" basis, Myriad's BRACAnalysis test costs less than testing for other genes performed by the GDL at the University of Pennsylvania and Drs. Ledbetter and Warren at Emory University. See infra; Critchfield Decl. ¶ 35.

3. Myriad's enforcement of the patents-in-suit

During the mid-to-late-1990s, Drs. Kazazian and Ganguly offered, for a fee, screening services for *BRCA1* mutations through the GDL at the University of Pennsylvania. Kazazian Decl. ¶ 4; Ganguly Decl. ¶ 3. The screening methodology utilized by Drs. Kazazian and Ganguly differed from the testing method used by Myriad, but involved using isolated DNA encoding *BRCA1* or *BRCA2*. Kazazian Decl. ¶ 9; Parthasarathy Decl. ¶ 23. At some point during this period, Dr. Skolnick advised Dr. Kazazian that Myriad planned to stop the *BRCA1/2* testing being

conducted at the GDL. Kazazian Decl. ¶ 6. On May 29, 1998, Myriad offered Dr. Kazazian a collaborative license in connection with the '473, '999, '001, '282, and '441 patents. Ganguly Decl. Ex. 2. However, the license covered only single mutation tests and multiple mutation panels of up to four mutations to allow for testing of patients of Ashkenazi Jewish descent. Ganguly Decl. ¶ 5. Myriad subsequently sent cease and desist letters to Dr. Kazazian and the University of Pennsylvania. On August 26, 1998, O'Melveny & Myers LLP gave notice to Dr. Kazazian of infringement in the absence of a license. Ganguly Decl. Ex. 3. Myriad subsequently sued the University of Pennsylvania in November 1998 for infringement of the patents-in-suit. See Myriad Genetics v. Univ. of Pennsylvania, 2:98-cv-00829 (D. Utah) (filed November 19, 1998). On June 10, 1999, Myriad's general counsel, Christopher Wright, sent a letter to the University of Pennsylvania seeking written assurances that Dr. Kazazian and the University of Pennsylvania had ceased *BRCA1/2* clinical testing. Ganguly Decl. Ex. 4. This demand was repeated in a September 22, 1999 letter from Myriad to the University of Pennsylvania. Ganguly Decl. Ex. 6.

As a result of Myriad's efforts to enforce its patents against the University of Pennsylvania, the GDL no longer conducts *BRCA1/2* screening for research or as part of its clinical practice. Kazazian Decl. ¶ 5; Ganguly Decl. ¶¶ 8-9; Parthasarathy Decl. ¶ 28. However, sometime between 1999 and 2000, Dr. Critchfield, on behalf of Myriad, informed Dr. Kazazian that he is free to conduct academic research on the *BRCA1/2* genes, including sequencing the genes and detecting mutations in the genes. Critchfield Decl. ¶ 22.

In May 1998, Myriad offered Dr. Ostrer a license agreement to conduct diagnostic *BRCA1/2* genetic testing. The proposed license would permit Dr. Ostrer to conduct single mutation tests and multiple mutation panels (up to four mutations) for patients of Ashkenazi Jewish descent only. Dr. Ostrer declined the offer as too narrow to allow him to perform any meaningful *BRCA1/2* testing. Ostrer Decl. ¶ 7.

On September 15, 1998, Myriad also notified Dr. Barbara Weber ("Dr. Weber"), a principal investigator on the Cancer Genetics Network Project ("CGNP") sponsored by the National Cancer Institute ("NCI"), that Myriad's patent

position might impact research sponsored by NCI. As a result of that letter, the GDL at the University of Pennsylvania ceased conducting *BRCA1/2* analysis for Dr. Weber. Ganguly Decl. ¶ 12, Ex. 7. According to Myriad, the GDL's involvement in CGNP was to provide DNA testing on *BRCA1/2* genes for a fee, similar to the activity of any commercial core lab. Critchfield Decl. ¶ 21. In September 1999, Myriad also requested that Georgetown University, one of the other cancer centers participating in the CGNP, to cease sending genetic samples to the GDL for *BRCA1/2* analysis. Ganguly Decl. ¶ 13.

In December 2000, the director of the Yale DNA Diagnostics Lab received a cease and desist letter concerning *BRCA1/2* genetic testing being conducted by the lab. As a result of the letter, the lab ceased *BRCA1/2* genetic testing. Matloff Decl. ¶ 7. In 2005, Dr. Matloff sought permission from Myriad for the Yale DNA Diagnostics Lab to conduct screening for mutations caused by large rearrangements, which Myriad was not conducting at the time. Her request was denied. Matloff Decl. ¶ 8.

Myriad was also involved in a series of lawsuits in the late 1990s against Oncormed, another company

undertaking *BRCA*-related testing, regarding patents that covered various aspects of the *BRCA1* gene sequence. Parthasarathy Decl. ¶ 27. Myriad eventually purchased Oncormed's patents and testing services in 1998. Id.

E. Disputed Issues

1. The impact of Myriad's patents on *BRCA1/2* testing

According to Plaintiffs, Myriad's patents and its position as the sole provider of *BRCA1/2* testing has hindered the ability of patients to receive the highest-quality breast cancer genetic testing and has impeded the development of improvements to *BRCA1/2* genetic testing. Plaintiffs first note deficiencies in the genetic testing services offered by Myriad, alleging that in the several years prior to the addition of the LRP, the testing done by Myriad did not reveal all known mutations in the *BRCA1/2* genes or utilize known methodologies that would have revealed these additional mutations.[21] Chung Decl. ¶ 19; Matloff Decl. ¶ 8; Swisher Decl. ¶ 26; Ledbetter Decl. ¶ 16; Parthasarathy Decl. ¶ 29. As a result, Myriad's test

[21] For example, the Myriad test received by Ms. Thomason, Ms. Raker, and Ms. Limary did not look for all known large rearrangements in the *BRCA* genes. Thomason Decl. ¶ 6; Raker Decl. ¶¶ 7-8; Limary Decl. ¶ 7.

may have reported false negative results during this period. Plaintiffs also cite a study published in 2006 in the Journal of the American Medical Association that concluded that 12% of those from high risk families with breast cancer and with negative test results from Myriad carried cancer-predisposing genomic deletions or duplications in one of those genes. Swisher Decl. ¶¶ 25-26. Plaintiffs also note that the sensitivity and specificity of the BART test has not been validated by comparing the results of BART testing with Multiplex Ligation Dependent Probe Amplification ("MLPA") testing commonly used by researchers. Swisher Decl. ¶¶ 32, 33.

According to Plaintiffs, other labs are in a position to offer more comprehensive testing than Myriad's standard testing services and would use newer testing methods with improved testing quality and efficiency. These labs would also include large rearrangement testing after a negative test result is received from full sequencing. Ledbetter Decl. ¶¶ 17-18; Chung Decl. ¶ 18; Ostrer Decl. ¶ 9. In addition, labs would perform genetic testing on tumor specimens preserved in paraffin from deceased family members, which Myriad does not regularly perform even though, according to Plaintiffs, such testing

can often provide valuable genetic information for living relatives and is often necessary for accurate test interpretation. Chung Decl. ¶ 24.

According to Myriad, however, its full sequencing test has been recognized as the "gold standard" for *BRCA1/2* mutation testing, and it continues to improve its testing process. Critchfield Decl. ¶ 37. Myriad contends that it researched and developed a commercially viable high quality test for detecting large rearrangements as soon as it and the research community recognized the need for such testing, and continues work towards a test capable of detecting all large rearrangement mutations, including extremely rare ones. Critchfield Decl. ¶¶ 49, 50. According to Myriad, *BRCA1/2* studies conducted by outside researchers confirmed that the BART test exhibited superior performance over other methods for mutation detection, including the MLPA kit often used by academic researchers.[22] Critchfield Decl. ¶ 51.

According to Plaintiffs, the lack of independent *BRCA1/2* analysis also undermines the ability of the

[22] In addition, Myriad states that the MLPA kit is for research use only, is not approved for clinical testing by the FDA, and is incapable of detecting certain smaller rearrangements. Critchfield Decl. ¶¶ 49, 50.

scientific community to determine the meaning of VUS results, which are reported disproportionately for members of minority groups, and whose significance would be more extensively analyzed by other labs. Chung Decl. ¶ 20-21; Ostrer Decl. ¶ 12; Matloff Decl. ¶ 9. Myriad, however, asserts that it has undertaken significant efforts to determine the clinical importance of VUSs by establishing an in-house review committee for variant classification and developing a systematic approach to providing clinical interpretations for detected sequence variants based on generally accepted scientific data and analysis of its own database. In addition, clarification of any VUS previously reported to a patient is immediately provided to the patient and her doctor. According to Myriad, the VUS reporting rate has decreased markedly, with a 50% decrease in major ethnic groups between 2002 and 2006, and a total of 850 VUSs for about 21,000 patients have been clarified, including 502 VUSs for 13,127 patients since the beginning of 2008. Myriad also asserts that it has made critical data available to researchers to assist in the analysis of VUSs and which have the potential of improving the diagnostic testing for other genes. Critchfield Decl. ¶¶ 57-59.

Plaintiffs contend that as a result of the patents-in-suit, *BRCA1/2* genetic testing is one of the very few tests performed as part of breast cancer care and prevention for which a doctor or patient cannot get a second confirmatory test done through another laboratory. Love Decl. ¶ 12. In particular, women who receive a positive result cannot confirm the lab's findings or seek a second opinion on the interpretation of those results.[23] Ledbetter Decl. ¶ 23; Ostrer Decl. ¶ 11. According to Myriad, absent any doubts regarding the accuracy of the original test, resequencing the patient's genes by another laboratory would be an unnecessary waste of resources, and Myriad has never prohibited a second interpretation of the results of its diagnostic tests. Critchfield Decl. ¶ 64; Reilly Decl. ¶¶ 54, 55. In addition, there are multiple laboratories available to conduct confirmatory *BRCA1/2* testing pursuant to patent licenses granted by Myriad, including both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Critchfield Decl. ¶ 62. That confirmatory testing,

[23] For example, Ms. Girard sought but was unable to obtain confirmatory testing of her Myriad test results that indicated the presence of a deleterious mutation in her *BRCA2* gene. A second opinion would also be important for her immediate family's screening options. Girard Decl. ¶¶ 4-9. Similarly, Ms. Ceriani and Ms. Fortune would both want a second opinion concerning their *BRCA1/2* status before taking major surgical steps. Ceriani Decl. ¶¶ 9, 11; Fortune Decl. ¶ 7.

however, is limited to the confirmation of certain, specific positive test results; the remaining types of positive test results as well as all negative test results are excluded from such testing services. Matloff Decl. ¶¶ 9, 10.

Whether the patents at issue impact the testing for *BRCA1/2* mutations favorably or unfavorably is an issue of factual dispute not resolvable in the context of the instant motions.

2. The impact of gene patents on the advancement of science and medical treatment

There exists a deep disagreement between the parties concerning the effects of gene patents on the progression of scientific knowledge.

According to Plaintiffs, data sharing is the key to the future of genetic discoveries and bioinformatics, and gene patents impede research aimed at identifying the role of genes in medical conditions. Sulston Decl. ¶¶ 36, 38. Plaintiffs assert that this understanding has wide acceptance, noting that from the beginning of the Human

Genome project,[24] most scientists and even some private companies recognized the importance of keeping the genome freely available to all. For example, in 1994, the pharmaceutical company Merck funded a massive drive to generate gene sequences and place them into public databases, thereby making them difficult to patent. Sulston Decl. ¶¶ 22, 29. In 1996, a group of 50 of the most prominent geneticists who were involved with the sequencing of the human genome adopted the Bermuda principles which included the mandate that all "human genome sequence information should be freely available and in the public domain in order to encourage research and development and to maximize its benefit to society." Sulston Decl. ¶ 33. The proliferation of intellectual property rights directed to genetic material has also been postulated to contribute to a phenomenon dubbed "the tragedy of the anti-commons," in which numerous competing patent rights held by independent parties prevents any one party from engaging in productive innovation. See, e.g., Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698 (1998) (citing Michael A. Heller, The Tragedy

[24] The Human Genome Project was an international project initiated in 1990 with the aim of sequencing an entire human genome and in which Sir John Sulston, a Nobel laureate, actively participated. Sulston Decl. ¶¶ 5, 22.

of the Anticommons: Property in the Transition from Marx to Markets, 111 Harv. L. Rev. 621 (1998)).

According to Dr. Fiona Murray ("Dr. Murray"), who received a grant to research the impact of gene patenting on scientific research and commercialization, 4382 of the 23,688 genes listed in the database of the National Center for Biotechnology Information ("NCBI") - nearly 20% of human genes - are explicitly claimed as United States intellectual property. Murray Decl. ¶ 6. After devising a study to gauge the impact of gene patenting on public knowledge that utilized the time lag between publication of papers on a gene sequence and the issuance of a patent claiming that gene sequence, Dr. Murray concluded that the Myriad patents have negatively impacted the public knowledge of the *BRCA1* and *BRCA2* genes by 5-10%. Murray Decl. ¶¶ 7-15, 20.

Plaintiffs have cited other studies to demonstrate the chilling effect of gene patents on the advancement of both genetic research and clinical testing. A survey of laboratory directors in the United States conducted by Dr. Mildred Cho (the "Cho study") found that 53% decided not to develop a new clinical test because of a

gene patent or license, and 67% believed that gene patents decreased their ability to conduct research. Cho Decl. ¶ 10. This correlated with a study conducted by the American Society of Human Genetics that reported that 46% of respondents felt that patents had delayed or limited their research. Cho Decl. ¶ 11. The Cho study also revealed that of those who stopped performing a clinical test because of a gene patent or license, the largest number stopped doing *BRCA1* and *BRCA2* testing (with the same number having stopped Apolipoprotein E testing). Cho Decl. ¶ 16. Specifically, the survey found that nine labs had ceased performing *BRCA1/2* genetic testing as a result of the patents-in-suit. In addition to labs that have ceased performing *BRCA1/2* genetic testing, labs have avoided or refrained from developing tests for *BRCA1* and *BRCA2* as a result of the patents held by Myriad. Ostrer Decl. ¶ 6; Ledbetter Decl. ¶¶ 14-16. Studies of other gene patents have also revealed that labs frequently stop developing or offering clinical tests for disease as a result of gene patents. For example, a purportedly valid scientific survey of labs in the United States found a 26% drop in the number of labs performing testing for hemochromatosis as a result of gene patents. Cho Decl. ¶¶ 18-20.

Researchers, clinicians, and pathologists are aware that Myriad has sent cease and desist letters in connection with the patents-in-suit and that Myriad prohibits clinical testing of the *BRCA1/2* genes. Kazazian Decl. ¶¶ 5-11; Ganguly Decl. ¶¶ 4-14; Chung Decl. ¶ 15; Hegde Decl. ¶ 10; Matloff Decl. ¶¶ 5-7; Ostrer Decl. ¶¶ 4-7; Swisher Decl. ¶ 28; Hubbard Decl. ¶¶ 7-8; Kant Decl. ¶ 4; Ledbetter Decl. ¶ 13; Reich Decl. ¶¶ 3, 5; Parthasarathy Decl. ¶¶ 28-31. Myriad also does not permit researchers to tell patients involved in research the results of their *BRCA1/2* testing, leading physicians involved in breast cancer care and research unable to meet their ethical obligations to provide genetic test results to research subjects, when requested. Ostrer Decl. ¶ 10; Chung Decl. ¶ 13, 14. In addition to the direct benefits to the patient of knowing the results of their testing, such disclosure would also provide valuable insights into patient behavior that would enhance patient care. Ostrer Decl. ¶ 10. The AMA has also expressed its belief that the "[t]he use of patents . . . or other means to limit the availability of medical procedures places significant limitation on the dissemination of medical knowledge, and is therefore unethical." American Medical Association, Opinion 9.095 - The Use of Patents and Other Means to Limit Availability of

Medical Procedures, (adopted June 1995), available at http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion9095.shtml. In addition, others have argued that human genes are the common heritage of mankind whose use should not be restricted by patent grants. See, e.g., Pilar A. Ossorio, The Human Genome as Common Heritage: Common Sense or Legal Nonsense?, 35 J.L. Med. & Ethics 425, 426 (2007); Melissa L. Sturges, Who Should Hold Property Rights to the Human Genome? An Application of the Common Heritage of Humankind, 13 Am. U. Int'l L. Rev. 219, 245 (1997); Barbara Looney, Should Genes Be Patented? The Gene Patenting Controversy: Ethical and Policy Foundations of an International Agreement, 26 Law & Pol'y Int'l Bus. 231 (1994); Hubert Curien, The Human Genome Project and Patents, 254 Science 1710, 1710-12 (1991).

According to Plaintiffs, Myriad has withheld critical data concerning genetic predisposition to breast cancer from the Breast Cancer Information Core ("BIC"), an international, open access online database that is a central repository for information about the *BRCA1/2* genes and their genetic variants. The BIC facilitates the identification of deleterious mutations (i.e. those

associated with a higher risk of cancer), provides a mechanism to collect and distribute data about genetic variants, and plays an important role in helping to elucidate the significance of those variants through its collection of data. Swisher Decl. ¶¶ 15, 17, 18; Chung Decl. ¶ 22; Ostrer Decl. ¶ 13. Although the value of the BIC comes from the amount and quality of data provided by the scientific community, Myriad, according to Plaintiffs, has not contributed any data to BIC in the past two years. Sulston Decl. ¶ 36; Swisher Decl. ¶¶ 19-21; Ostrer Decl. ¶¶ 12-13; Chung Decl. ¶¶ 21-22; Ledbetter Decl. ¶ 20.

Plaintiffs also assert that gene patents impede the development of improved genetic testing. For example, as new sequencing technologies offer the possibility of faster and less expensive sequencing of a patient's genes, patents on one or more genes may impede scientists' ability to develop a comprehensive test for complex diseases or provide a person with an analysis of his or her entire genome. Sulston Decl. ¶ 38; Ledbetter Decl. ¶ 24. In addition, Plaintiffs assert that gene patents interfere with the ability of physicians and researchers to investigate complex diseases. For example, *BRCA1/2* may be associated with cancers other than breast and ovarian

cancer, but so long as the patents on these genes remain, no one will be able to include these genes in tests for other disease predispositions. Ledbetter Decl. ¶¶ 24-25. Gene patents similarly impede the development and improvement of tests for diseases by geneticists. Ledbetter Decl. ¶¶ 14-15. Plaintiffs also assert that allowing only a single lab to offer testing means that the one lab dictates the standards for patient care in testing for that disease; in contrast, patient care is promoted when more than one lab offers a particular genetic test, utilizing different methodologies, since this can ensure the quality of the testing and accuracy of the test results. Chung Decl. ¶ 23; Ledbetter Decl. ¶ 23; Reich Decl. ¶¶ 9, 11; Ostrer Decl. ¶ 11; Parthasarathy Decl. ¶ 31.

Plaintiffs further assert that gene patents are not necessary to create incentives for initial discoveries or the development of commercial applications, including diagnostic tests. Cho Decl. ¶ 25; Leonard Decl. ¶¶ 20-21. Patents have not been necessary for the rapid introduction of genetic testing, as evidenced by genetic testing that has been offered prior to the issuance of a patent. Cho Decl. ¶ 21. In support of this assertion, Plaintiffs cite

a study of gene patents issued in the United States for genetic diagnostics that showed that 67% of these patents were issued for discoveries funded by the U.S. government. Cho Decl. ¶ 22. Similarly, another study showed that 63% of patents on gene sequences resulted from federally supported research. Leonard Decl. ¶ 22. As previously noted, the NIH provided $2 million in research grants to the University of Utah, or approximately one-third of the total funding, for the identification of the *BRCA1* sequence. Parthasarathy Decl. ¶ 18.

Myriad has contested these assertions and disputes the idea that patenting of isolated human DNA conflicts with the advancement of science. According to Myriad, the quid pro quo of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly Decl. ¶ 24; Doll Decl. ¶ 44. Furthermore, according to Myriad, its policy and practice has been and still is to allow scientists to conduct research studies on *BRCA1* and *BRCA2* freely, the result of which has been the publication of over 5,600 research papers on *BRCA1* and over 3,000 research papers on *BRCA2*, representing the work of over

18,000 scientists. Critchfield Decl. ¶¶ 3, 13; Li Decl. ¶¶ 3-6; Baer Decl. ¶¶ 3-6; Parvin Decl. ¶¶ 3-6; Sandbach Decl. ¶¶ 3-7.

According to Myriad, patents on isolated DNA, including the patents-in-suit, actually promote research and advance clinical development to the benefit of patients. Reilly Decl. ¶¶ 38, 43; Critchfield Decl. ¶¶ 2-18, 65, 68; Linck Decl. ¶¶ 27-28, 71, 73; Tavtigian Decl. ¶¶ 14-17; Doll Decl. ¶¶ 45-46; Schlessinger Decl. ¶¶ 31-32. Myriad has contended that gene patents are essential for obtaining capital investment in the development and commercialization of technological breakthroughs. Linck Decl. ¶¶ 27, 28; Reilly Decl. ¶ 16; Doll Decl. ¶ 46. In support, Myriad has cited a survey published in 2009 by the BIO of 150 biotechnology member companies in the therapeutic and diagnostic healthcare industry stating that the majority of companies (61%) generally in-licensed projects that are in the pre-clinical or Phase I stage of development, and thus still require substantial R&D investment and commercialization risk by the licensee. A substantial majority (77%) of the respondents without approved products indicated that they expect to spend 5-15 years and over $100 million developing a commercial

product. Myriad asserts that these expenditures dwarf any initial research funding by the federal government. Reilly Decl. ¶ 22. In particular, Myriad notes that a significant amount of private investment led to its identification of the *BRCA1* and *BRCA2* sequences, with the expectation of patent protection providing an incentive to fund the research into the determination of the gene sequences. Skolnick Decl. ¶¶ 14-16. Therefore, Myriad asserts that absent the promise of a period of market exclusivity provided by patents and the infusion of venture and risk capital derived therefrom, companies such as Myriad that capitalize on innovation simply would not be created and their products would not be brought to market or the clinic. Reilly Decl. ¶¶ 18, 34, 51, 52, 62; Critchfield Decl. ¶¶ 67, 68; Linck Decl. ¶ 73.

Myriad also notes that it has made over 20,000 submissions to the BIC database, making it the largest contributor to the database. It has also published the largest clinical series of mutation risk in the *BRCA1/2* genes based on its testing data and has tabulated and posted the data on Myriad's website, where it is freely available to researchers throughout the world. Critchfield Decl. ¶¶ 11, 12.

According to Myriad, the majority of academic researchers operating laboratories (as opposed to Clinical Laboratory Improvement Amendments ("CLIA")-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly Decl. ¶¶ 57-59.

As the declarations submitted by the parties make clear, there exists a sharp dispute concerning the impact of patents directed to isolated DNA on genetic research and consequently the health of society. As with the dispute concerning the effect of the patents-in-suit on *BRCA1/2* genetic testing, the resolution of these disputes of fact and policy are not possible within the context of these motions.

IV. THE PATENTS

A. Summary of the Patents

The subjects of this declaratory judgment action are fifteen claims contained in seven patents issued by the

USPTO:[25] claims 1, 2, 5, 6, 7, and 20 of U.S. patent 5,747,282 (the "'282 patent"); claims 1, 6, and 7 of U.S. patent 5,837,492 (the "'492 patent"); claim 1 of U.S. patent 5,693,473 (the "'473 patent"); claim 1 of U.S. patent 5,709,999 (the "'999 patent"); claim 1 of U.S. patent 5,710,001 (the "'001 patent"); claim 1 of U.S. patent 5,753,441 (the "'441 patent"); and claims 1 and 2 of U.S. patent 6,033,857 (the "'857 patent").[26]

The claims-in-suit may be divided into two types of claims: composition claims and method, or process, claims. Independent claim 1 of the '282 patent is representative of the group of composition claims and claims:

> An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

This claim is therefore directed to an isolated DNA

[25] The USPTO granted these patents pursuant to a formal written policy that permits the patenting of "isolated and purified" DNA encoding human genes and pursuant to a practice that permits such DNA patents and the patenting of correlations created by nature between natural elements of the body and a predisposition to disease. See Utility Examination Guidelines, 66 Fed. Reg. 1,093 (Jan. 5, 2001).

[26] For purposes of understanding what the claim terms would have meant to a person of ordinary skill in the art at the time of the application for the patents, an application date of August 1994 is presumed for the '282, '473, '999, '001, and '441 patents and December 1995 for the '492 and '857 patents.

molecule possessing a nucleotide sequence that translates into the BRCA1 protein. Because most amino acids can result from the translation of more than one DNA codon, multiple DNA sequences correspond to the nucleotide sequence claimed by this claim. Claim 2 of the '282 patent is dependent on claim 1 but contains an additional limitation that identifies the specific *BRCA1* nucleotide sequence of the claimed DNA.[27] Claims 5 and 6 of the '282 patent are directed to fragments as short as 15 nucleotides of the DNA molecules claimed in claims 1 and 2 of the '282 patent.[28] Finally, claim 7 of the '282 patent and claim 1 of the '473 patent are directed to isolated DNA possessing one of the specified mutant *BRCA1* gene sequences.[29]

Claims 1, 6, and 7 of the '492 patent are also

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[27] Claim 2 of the '282 patent reads: "The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

[28] Claim 5 of the '282 patent claims: "An isolated DNA having at least 15 nucleotides of the DNA of claim 1."
Claim 6 of the '282 patent reads: "An isolated DNA having at least 15 nucleotides of the DNA of claim 2."

[29] Claim 7 of the '282 patent reads: "An isolated DNA selected from the group consisting of: (a) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having T at nucleotide position 4056; (b) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having an extra C at nucleotide position 5385; (c) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having G at nucleotide position 5443; and (d) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having 11 base pairs at nucleotide positions 189-199 deleted."
Claim 1 of the '473 patent reads: "An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in Tables 12A, 14, 18 or 19 with the proviso that the alteration is not a deletion of four nucleotides corresponding to base numbers 4184-4187 in SEQ. ID. NO:1."

composition claims covering isolated DNA molecules containing certain specified nucleotide sequences relating to the *BRCA2* gene. Claim 1 is directed to an isolated DNA molecule encoding the BRCA2 protein.[30] Like claim 1 of the '282 patent, claim 1 of the '492 patent is directed to multiple possible DNA sequences as a result of the redundancy of the DNA codons. Claim 6 of the '492 patent, however, is considerably broader than claim 1 and is directed to any DNA nucleotide encoding any mutant BRCA2 protein that is associated with a predisposition to breast cancer.[31] Claim 7 of the '492 patent depends on claim 6, but is restricted to the mutated forms of the *BRCA2* nucleotide sequence set forth in the specification.[32] As a result of the breadth of these composition claims, they reach isolated *BRCA1/2* DNA obtained from any human being.

Claim 1 of the '999 patent is representative of the group of method claims. It claims:

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[30] Claim 1 of the '492 patent reads: "An isolated DNA molecule coding for a BRCA2 polypeptide, said DNA molecule comprising a nucleic acid sequence encoding the amino acid sequence set forth in SEQ ID NO:2."
[31] Claim 6 of the '492 patent reads: "An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer."
[32] Claim 7 of the '492 patent reads: "The isolated DNA molecule of claim 6, wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID cNO:1."

> A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from a group consisting of the alterations set forth in Tables 12A, 14, 18, or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1.

Thus, claim 1 of the '999 patent covers the process of identifying the existence of certain specific mutations in the *BRCA1* gene by "analyzing" the sequence of the *BRCA1* DNA, RNA, or cDNA made from *BRCA1* RNA obtained from a human sample.

Most of the remaining method claims-in-suit are similarly structured and directed to the comparison of gene sequences. Claim 1 of the '001 patent claims a method for determining whether a human tumor sample contains a mutation in the *BRCA1* gene by "comparing" the sequence of the *BRCA1* gene from the tumor with the sequence of the *BRCA1* gene from a non-tumor sample from the same person.[33]

[33] Claim 1 of the '001 patent reads: "A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises gene comparing a first sequence selected form [sic] the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group

Claim 1 of the '441 patent and claim 1 of the '857 are both directed to the same process, differing only as to whether the claimed method is directed to *BRCA1* ('441) or *BRCA2* ('857). Both of these independent claims are directed to the process of determining whether an individual has inherited an altered *BRCA1* or *BRCA2* gene by "comparing" the individual's *BRCA1* or *BRCA2* gene sequence with the wild-type *BRCA1* or *BRCA2* gene sequence.[34] Claim 2 of the '857 patent covers a method for determining whether an individual has a predisposition for breast cancer by "comparing" the individual's *BRCA2* gene sequence with the known wild-type *BRCA2* gene sequence.[35]

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consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample."

[34] Claim 1 of the '441 patent reads: "A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject." Claim 1 of the '857 patent claims: "A method for identifying a mutant BRCA2 nucleotide sequence in a suspected mutant BRCA2 allele which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence, wherein a difference between the suspected mutant and the wild-type sequences identifies a mutant BRCA2 nucleotide sequence."

[35] Claim 2 of the '857 patent reads: "A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the

Finally, claim 20 of the '282 patent claims a method for determining the effectiveness of a potential cancer therapeutic comprising growing cells carrying an altered *BRCA1* gene known to cause cancer in the presence and absence of a potential cancer therapeutic, comparing the growth rates of the cells, and concluding that a slower growth rate in the presence of the potential therapeutic indicates that it is indeed a cancer therapeutic.[36]

B. Construction of the Claims[37]

1. Legal standard

Before considering the patent-eligibility of a patent claim, the disputed terms in the claims must be

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sequence of its mRNA of the subject indicates a predisposition to said cancer."

[36] Claim 20 of the '282 patent reads: "A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer n the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic."

[37] In addition to the claim terms discussed below, the parties also dispute the proper interpretation of the method claims - i.e., whether they may be construed to encompass certain transformative steps. Because this issue is broader in scope than simple claim term definition, it is addressed *infra* in Section VII.D.

construed in order ensure the scope of the claims is accurately assessed. See, e.g., Datamize, LLC v. Plumtree Software, Inc., 417 F.3d 1342, 1354 (Fed. Cir. 2005) ("[A] utility patent protects 'any new and useful process, machine, manufacture, or composition of matter, or any new or useful improvement thereof,' 35 U.S.C. § 101 (2000), the scope of which is defined by the patent's written claims."). Courts are charged with interpreting disputed claim terms as a matter of law. Markman v. Westview Instruments, Inc., 517 U.S. 370, 384-85 (1996).

In interpreting the meaning of claim terms, "words of a claim are generally given their ordinary and customary meaning" to a person of ordinary skill in the art at the time of invention (i.e., the effective filing date of the patent application). Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (internal citations and quotation marks omitted). "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." Id. at 1313. Thus, the Federal Circuit has emphasized the importance of "intrinsic" evidence in claim construction: the words of

the claim themselves, the written description in the patent's specification, and, when necessary, the history of the patent application's prosecution before the USPTO. Id. at 1314-17.

The process of claim construction begins with the language of the claims themselves. The language of the claim is what the patentee chose to use to "'particularly point[] out and distinctly claim[] the subject matter which the applicant regards as his invention.'" Id. at 1311-12 (quoting 35 U.S.C. § 112, ¶ 2). Thus, "the claims themselves provide substantial guidance as to the meaning of particular claim terms." Id. at 1314. In addition to the particular claim being examined, the context provided by other claims may be helpful as well. "For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." Id. at 1314-15.

Claim language must also be read in the context of the specification. Id. at 1315. As the Federal Circuit has made clear, "claims, of course, do not stand alone. Rather, they are part of 'a fully integrated written

instrument,' consisting principally of a specification that concludes with the claims." Id. (quoting Markman v. Westview Instruments, Inc., 52 F.3d 967, 978 (Fed. Cir. 1995)). "For that reason, claims 'must be read in view of the specification, of which they are a part.'" Id. (quoting Markman, 52 F.3d at 979). The specification "is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term." Id. (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Moreover, when the patentee "act[s] as his or her own lexicographer" and includes an explicit definition of a claim term in the specification, that definition is dispositive over any ordinary meaning. Id. at 1319 (internal citation and quotation marks omitted); see also Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed. Cir. 1998).

In relying on the specification to interpret claim terms, the Federal Circuit has also "repeatedly warned against confining the claims" to the embodiments described in the specification. Phillips, 415 F.3d at 1323. The mistake of "reading a limitation from the written description into the claims" is "one of the

cardinal sins of patent law." Id. at 1320 (quoting SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1340 (Fed. Cir. 2001)).

Courts may also utilize the prosecution history which "consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent . . . . [T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id. at 1317 (internal citations omitted). However, the prosecution history "often lacks the clarity of the specification and thus is less useful for claim construction purposes." Id.

Lastly, courts may rely on extrinsic evidence such as dictionaries, treatises, and expert testimony, which may serve to provide a source of "accepted meaning of terms used in various fields of science and technology," or by providing "background on the technology at issue." Id. at 1317-18. However, such "extrinsic" evidence is "less significant than the intrinsic record in determining the

legally operative meaning of the claim language." Id. at 1317 (internal citations and quotation marks omitted). The use of extrinsic evidence may not be used to contradict the meaning of the claim terms as evidenced by the intrinsic evidence. Id. at 1317-19; see also Biagro W. Sales, Inc. v. Grow More, Inc., 423 F.3d 1296, 1302 (Fed. Cir. 2005).

2. Resolution of the disputed claim terms

a. "DNA" and "isolated DNA"

The parties approach the terms "DNA" and "isolated DNA" from opposing perspectives.[38] Plaintiffs contend that the term "DNA" means "a sequence of nucleic acids, also referred to as nucleotides" and therefore constitutes a "nucleotide sequence" or a "polynucleotide." Pl. Br. at 10.[39] Myriad disputes Plaintiffs' definition of

[38] The degree to which the parties actually disagree on the meaning of the discussed claim terms is unclear; however, to the extent some disagreement has been noted by the parties, this section seeks to resolve them.

[39] For purposes of this opinion, "Pl. Br." refers to Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment; "Myriad Br." refers to Myriad Defendants' Memorandum of Law (1) in Support of Their Motion for Summary Judgment and (2) in Opposition to Plaintiffs' Motion for Summary Judgment; "Pl. Reply" refers to the Memorandum of Law (1) in Further Support of Plaintiffs' Motion for Summary Judgment Against All Defendants and (2) in Opposition to the Myriad Defendants' Motion for Summary Judgment and (3) in Opposition to Defendant United States Patent and Trademark Office's Motion for Judgment on the Pleadings; "Myriad Reply" refers to Myriad Defendants' Memorandum in Reply to Plaintiffs' Opposition to Myriad Defendants' Motion for

"DNA" insofar as Plaintiffs' definition suggests that the term "DNA" refers merely to information, that is, "a description of the linear order of nucleotide units that make up the polynucleotide." Myriad Br. at 15. Myriad instead argues that "DNA" refers to "a real and tangible molecule, a chemical composition made up of deoxyribonucleotides linked by a phosphodiester backbone." Myriad Br. at 14.

As its name implies, DNA, or deoxyribonucleic acid, is an acid - a tangible, chemical compound. As Myriad correctly notes, the specifications make clear that "DNA," as used in the patents, refers to the physical manifestation of the acid, one that may be "substantially separated from other cellular components which naturally accompany a gene." '473 patent, col. 19:8-9; '282 patent, col. 19:10-11; '492 patent, col. 17:64-65. Despite the description of the term "DNA" set forth in the briefs, this understanding of the meaning of "DNA" is shared by both Plaintiffs' and Myriad's declarants. See Kay ¶ 125; Linck ¶ 45; Schlessinger ¶ 12; Grody ¶ 10; Leonard ¶ 30.

Summary Judgment; and "USPTO Reply" refers to the Reply Memorandum of Law in Further Support of Defendant United States Patent and Trademark Office's Motion for Judgment on the Pleadings and in Opposition to Plaintiffs' Motion for Summary Judgment.

The term "isolated DNA" is defined by Plaintiffs as "a fragment of DNA substantially separated from other cellular components and other DNA." Pl. Br. at 10. Myriad disputes Plaintiffs' definition insofar as it implies that fragments of DNA exist free-floating in the cell, separate from other cellular components, such as proteins and the other DNA in the chromosome. Myriad Br. at 16. The patent specifications expressly define "isolated DNA" as a DNA molecule "which is substantially separated from other cellular components which naturally accompany a native human sequence [such as] human genome sequences and proteins" and "includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems." '473 patent, col. 19:6-15; '282 patent, col. 19:8-18; '492 patent, col. 17:62-18:5.

"Isolated DNA" is therefore construed to refer to a segment of DNA nucleotides existing separate from other cellular components normally associated with native DNA, including proteins and other DNA sequences comprising the remainder of the genome, and includes both DNA originating from a cell as well as DNA synthesized through chemical or heterologous biological means.

b. "BRCA1" and "BRCA2"

Plaintiffs define the term "BRCA1" as "a particular fragment of DNA found on chromosome 17 that relates to a person's predisposition to develop breast and ovarian cancer." Pl. Br. at 11. Similarly, Plaintiffs define the term "BRCA2" as "a particular fragment of DNA found on chromosome 13 that relate[s] to a person's predisposition to develop breast and ovarian cancer." Pl. Br. at 14. As with Plaintiffs' proposed definition of "isolated DNA," Myriad argues that these definitions are inconsistent with the patents' definition of "BRCA1" and "BRCA2" as "cancer-predisposing gene[s], some alleles of which cause susceptibility to breast and ovarian cancers" because they suggest that the *BRAC1* and *BRCA2* genes are not integrated into a chromosome, but are broken, detached, or otherwise easily removed from their respective chromosomes. Myriad Br. at 16.

The specifications of the patents-in-suit define the terms "BRCA1" and "BRCA2" as "a human breast cancer predisposing gene . . . some alleles of which cause

susceptibility to cancer, in particular breast and ovarian cancer." '282 patent, col. 4:33-36; see also '282 patent, col. 1:22-23; '492 patent, col. 1:20-21, 4:28-29. Further, neither party disputes that "genes" refer to segments of DNA incorporated into chromosomes.

"BRCA1" is therefore construed to refer to a human gene, normally integrated into chromosome 17, some alleles of which cause susceptibility to breast and ovarian cancer. Similarly, "BRCA2" is construed to refer to a human gene, normally integrated into chromosome 13, some alleles of which cause susceptibility to breast and ovarian cancer.

V. CONCLUSIONS OF LAW

A. The Summary Judgment Standard

Summary judgment is granted only where there exists no genuine issue of material fact and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c); see Celotex Corp. v. Catrett, 477 U.S. 317, 322-23 (1986); SCS Commc'ns, Inc. v. Herrick Co., 360 F.3d 329, 338 (2d Cir. 2004). The courts do not try issues of

fact on a motion for summary judgment, but, rather, determine "whether the evidence presents a sufficient disagreement to require submission to a jury or whether it is so one-sided that one party must prevail as a matter of law." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 251-52 (1986).

"The party seeking summary judgment bears the burden of establishing that no genuine issue of material fact exists and that the undisputed facts establish [its] right to judgment as a matter of law." Rodriguez v. City of New York, 72 F.3d 1051, 1060-61 (2d Cir. 1995). In determining whether a genuine issue of material fact exists, a court must resolve all ambiguities and draw all reasonable inferences against the moving party. See Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587-88 (1986); Gibbs-Alfano v. Burton, 281 F.3d 12, 18 (2d Cir. 2002). However, "the non-moving party may not rely simply on conclusory allegations or speculation to avoid summary judgment, but instead must offer evidence to show that its version of the events is not wholly fanciful." Morris v. Lindau, 196 F.3d 102, 109 (2d Cir. 1999) (internal quotation marks omitted).

Summary judgment is appropriate where the moving party has shown that "little or no evidence may be found in support of the nonmoving party's case. When no rational jury could find in favor of the nonmoving party because the evidence to support its case is so slight, there is no genuine issue of material fact and a grant of summary judgment is proper." Gallo v. Prudential Residential Servs., L.P., 22 F.3d 1219, 1223-24 (2d Cir. 1994) (internal citations omitted).

B. 35 U.S.C. § 101 and Its Scope

Section 101 of Title 35, United States Code, provides:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

In interpreting this language, the Supreme Court has observed that "Congress plainly contemplated that the patent laws would be given wide scope." Diamond v.

Chakrabarty, 447 U.S. 303, 308 (1980); see also J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 131 (2001) ("[W]e are mindful that this Court has already spoken clearly concerning the broad scope and applicability of § 101.").

However, this broad reading of § 101 and statutory patent eligibility is not without limits. "The Supreme Court has recognized that scientific principles and laws of nature, even when for the first time discovered, have existed throughout time, define the relationship of man to his environment, and, as a consequence, ought not to be the subject of exclusive rights to any one person." In re Meyer, 688 F.2d 789, 795 (C.C.P.A. 1982) (citing Leroy v. Tatham, 55 U.S. 155, 175 (1852)). Specifically, the Supreme Court has recognized three categories of subject-matter that fall outside the scope of § 101: "The laws of nature, physical phenomena, and abstract ideas have been held not patentable." Chakrabarty, 447 U.S. at 309; see also Diamond v. Diehr, 450 U.S. 175, 185 (1981). "The rule that the discovery of a law of nature cannot be patented rests, not on the notion that natural phenomena are not processes, but rather on the more fundamental understanding that they are not the kind of 'discovery' that the statute

was enacted to protect." Parker v. Flook, 437 U.S. 584, 593 (1978).

The exclusion of products of nature[40] as patentable subject matter under § 101 also reflects the Supreme Court's recognition that "[p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." Gottschalk v. Benson, 409 U.S. 63, 67 (1972). Thus, as Justice Breyer has observed, "the reason for this exclusion is that sometimes *too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts,' the constitutional objective of patent and copyright protection." Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 126-27 (2006) (Breyer, J.,

[40] Myriad distinguishes between "laws of nature," "natural phenomena," and "abstract ideas," which it concedes are not patentable, and "products of nature," for which it appears to argue no prohibition to patentability exists. Although the distinction between these two categories is unclear, it is well established that "products of nature" are not patentable. See, e.g., Chakrabarty, 447 U.S. at 13 (stating that relevant distinction for § 101 patentability is "between products of nature, whether living or not, and human-made inventions"); Gen. Elec. Co. v. De Forest Radio Co., 28 F.2d 641, 642 (3d Cir. 1928) (noting that "a patent cannot be awarded for a discovery or for a product of nature, or for a chemical element"); In re Marden, 47 F.2d 957, 957 (C.C.P.A. 1931) (concluding that "[u]ranium is a product of nature, and the appellant is not entitled to a patent on the same, or upon any of the inherent natural qualities of that metal"); In re Marden, 47 F.2d 958, 959 (C.C.P.A. 1931) (stating that "pure vanadium is not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same").

dissenting) (quoting U.S. Const., Art. I, § 8, cl. 8.) (emphasis in original). For these reasons, "manifestations of laws of nature [are] free to all men and reserved exclusively to none." Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

The inquiry into an invention's patent eligibility is a fundamental one, and as such, "[t]he obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious." Flook, 437 U.S. at 593; see also In re Bilski, 545 F.3d 943, 950 (Fed. Cir. 2008) (en banc), cert. granted, 129 S. Ct. 2735 (2009) ("Whether a claim is drawn to patent-eligible subject matter under § 101 is a threshold inquiry, and any claim of an application failing the requirements of § 101 must be rejected even if it meets all of the other legal requirements of patentability." (citing In re Comiskey, 499 F.3d 1365, 1372 (Fed. Cir. 2007)); Prometheus Labs. v. Mayo Collaborative Servs., 581 F.3d 1336, 1343 (Fed. Cir. 2009) (noting that in determining patent eligibility, "it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements set forth in 35 U.S.C. §§ 102 and

103, respectively." (citing Bilski, 545 F.3d at 958)). Consistent with this approach, the courts have rejected patent claims even when the purported invention was highly beneficial or novel, or the research and work that went into identifying it was costly or time-consuming. See, e.g., Funk Bros., 333 U.S. at 130; Am. Fruit Growers, Inc. v. Brodgex Co., 283 U.S. 1, 11-13 (1931); Gen. Elec. Co. v. De Forest Radio Co., 28 F.2d 641, 642-43 (3d Cir. 1928).

The distinction between the § 101 inquiry into patentable subject matter and the other requirements for patentability set forth in Title 35 is of particular importance in evaluating the authorities cited by the parties and the arguments presented. The discussion of § 101 in In re Bergy, 596 F.2d 952 (C.C.P.A. 1979) by the late Honorable Giles S. Rich, one of the authors of the 1952 Patent Act, is particularly informative in clarifying the proper scope of a § 101 analysis. There, Judge Rich stated what considerations were salient - and importantly, what considerations were not - in a § 101 analysis:

> Section 101 states three requirements: novelty, utility, and statutory subject matter. The understanding that these three requirements are separate and distinct is long-standing and has been universally accepted. . . . Thus, the questions of whether a particular invention is

> novel or useful are questions wholly apart from whether the invention falls into a category of statutory subject matter. *Of the three requirements stated in § 101, only two, utility and statutory subject matter, are applied under § 101.* As we shall show, in 1952 Congress voiced its intent to consider the novelty of an invention under § 102 where it is first made clear what the statute means by "new," notwithstanding the fact that this requirement is first named in § 101.

Id. at 960-61 (emphasis added). Judge Rich further cautioned that "statements in the older cases must be handled with care lest the terms used in their reasoning clash with the reformed terminology of the present statute; lack of meticulous care may lead to distorted legal conclusions." Id. at 959. The Supreme Court subsequently affirmed this understanding of the § 101 analysis in Diehr, noting that while it had been argued that "novelty is an appropriate consideration under § 101," "[t]he question . . . of whether a particular invention is novel is 'wholly apart from whether from whether the invention falls into a category of statutory subject matter.'" 450 U.S. at 189-90 (quoting Bergy, 596 F.2d at 961); see also Bilski, 545 F.3d at 958 ("So here, it is irrelevant to the § 101 analysis whether Applicants' claimed process is novel or non-obvious.").

Accordingly, in considering whether the patents-in-suit comply with § 101, the proper analysis requires determining (1) whether the claimed invention possesses utility; and (2) whether the claimed invention constitutes statutory subject matter, that is, whether it is a "process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," 35 U.S.C. § 101, or whether the claimed invention instead falls within the judicially created "products of nature" exception to patentable subject matter, i.e., "laws of nature, natural phenomenon, and abstract ideas," Chakrabarty, 447 U.S. at 309. In contrast, the question of whether an invention is "new" or "novel" over the prior art is a question addressed by § 102 and falls outside of the scope of the present § 101 analysis. Because it is undisputed that the claimed compositions and methods possess utility, the sole task of this Court is to resolve whether the claimed compositions and methods constitute statutory subject matter or fall within the judicially created products of nature exception to patentable subject matter.

C. The Composition Claims Are Invalid Under 35 U.S.C. § 101

As noted, the issue presented by the instant motions with respect to the composition claims is whether or not claims directed to isolated DNA containing naturally-occurring sequences fall within the products of nature exception to § 101. Based upon the reasons set forth below, it is concluded that the composition claims-in-suit are excepted.

1. Consideration of the merits of Plaintiffs' challenge is appropriate.

Myriad offers several arguments for why this Court should not engage the substance of Plaintiffs' claims, but should instead dismiss them out of hand. Foremost among them is Myriad's assertion that Plaintiffs' claims should be dismissed in light of the "carefully considered policy of the USPTO," which is "entitled to great respect from the courts." Myriad Br. at 26. In so arguing, Myriad notes the presumption of validity afforded to patents, see 35 U.S.C. § 282, and the USPTO's prior consideration of the eligibility of gene-related patents, see Utility Examination Guidelines 66 Fed. Reg. 1092, 1092-99 (Jan. 5, 2001), as well as the Supreme Court's statements in J.E.M. Ag Supply, 534 U.S. 124.

The Federal Circuit has previously held that it owes no deference to USPTO legal determinations. See, e.g., Arnold P'ship v. Dudas, 362 F.3d 1338, 1340 (Fed. Cir. 2004) ("This court reviews statutory interpretation, the central issue in this case, without deference."). While Congress has created a presumption of validity for issued patents, approximately 40% of patents challenged in the courts have been found invalid, demonstrating that this presumption is far from absolute. See Institute for Intellectual Property & Information Law, University of Houston Law Center, Patstats.org, Full Calendar Year 2008 Report, http://www.patstats.org/2008_Full_Year_Posting.rev3.htm (indicating that 40% of all validity determinations in federal court in 2008 found the challenged patent invalid); Paul F. Morgan & Bruce Stoner, Reexamination v. Litigation - Making Intelligent Decisions in Challenging Patent Validity, 86 J. Pat. & Trademark Off. Soc'y 441-461 (2004) (citing USPTO statistics showing that 74% of patents previously issued by the Patent Office and later challenged through the reexamination process were either canceled or changed by the USPTO). Moreover, the lack of Congressional action to specifically prohibit gene patents in response to the USPTO's prior grant of such patents does not preclude

their review by the courts. For example, in Bilski, 545 F.3d 943, the Federal Circuit set out a test for the patentability of method claims that potentially will invalidate thousands of patents on business method patents, despite Congress' silence concerning the patentability of such methods. Finally, while the Supreme Court in J.E.M. Ag Supply noted the USPTO's practice of issuing patents on sexually reproducing plants in concluding that such plants represented patentable subject matter under § 101, that passing observation was neither dispositive nor central to the Court's holding and does not establish a rule of judicial deference to the USPTO's practices. See J.E.M. Ag Supply, 534 U.S. at 144-45. Indeed, the judicial deference urged by Myriad is difficult to reconcile with the courts' consideration of the substantive issues presented in cases such as Chakrabarty and indeed, J.E.M. Ag Supply itself.

Moreover, in the absence of a § 101 challenge to patent validity, the fact that courts have previously upheld the validity of patents directed to biological products in response to § 102 and/or § 103 challenges has no bearing on the present inquiry. See, e.g., In re Kubin, 561 F.3d 1351 (Fed. Cir. 2009) (considering obviousness of claims); In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988)

(same). The Patent Act sets out patent invalidity as an issue to be raised by the parties, see 35 U.S.C. § 282, and it would be erroneous to treat a case involving DNA-related patents as holding that isolated human genes constitute patentable subject matter under § 101. Were that the case, the Supreme Court could have proceeded with its consideration of Metabolite Labs., after it granted certiorari and the parties and amici had fully briefed the issue of patentable subject matter eligibility, rather than dismissing certiorari as improvidently granted based on the parties' failure to raise the § 101 issue below. 548 U.S. 124.

Finally, Myriad's suggestion that invalidating the patents-in-suit would constitute an unconstitutional taking in violation of the Fifth Amendment of the Constitution or a violation of the United States' obligations under the Agreement on Trade-Related Aspects of Intellectual Property Rights ("TRIPS") is unpersuasive. Myriad's novel takings argument runs counter to a long history of invalidation of patent claims by the courts and is unsupported by legal precedent. Similarly, Articles 8.1 and 27.3 of TRIPS permit governments to incorporate public health concerns into their intellectual property laws and

to exclude from patentability diagnostic, therapeutic, or surgical methods as well as particular inventions on the grounds of public interest. As a result, invalidation of the patents-in-suit would constitute neither a constitutional violation nor a conflict with the United States' treaty obligations.

2. Patentable subject matter must be "markedly different" from a product of nature

Supreme Court precedent has established that products of nature do not constitute patentable subject matter absent a change that results in the creation of a fundamentally new product. In American Fruit Growers, the Supreme Court rejected patent claims covering fruit whose skin had been treated with mold-resistant borax. Acknowledging that the "complete article is not found in nature," and "treatment, labor and manipulation" went into producing the fruit, the Court nonetheless held that the fruit did not become an "article of manufacture" unless it "possesses a new or distinctive form, quality, or property" compared to the naturally-occurring article.[41] 283 U.S. at 11. The Court went on to observe:

[41] Myriad argues that American Fruit Growers was decided on novelty grounds, rather than subject matter patentability. See Myriad Br. at 26. However, the Court's novelty discussion was restricted to its

> Manufacture implies a change, but every change is not manufacture, and yet every change in an article is the result of treatment, labor, and manipulation. But something more is necessary . . . . There must be transformation; a new and different article must emerge having a distinctive name, character, or use.

Id. at 12-13 (quoting Anheuser-Busch Brewing Ass'n v. United States, 207 U.S. 556, 562 (1908)) (internal citation and quotation marks omitted).

Similarly, in Funk Brothers, the Supreme Court considered whether a mixture of several naturally-occurring species of bacteria was patentable.[42] 333 U.S. at 128-31. Each species of bacteria in the mixture could extract nitrogen from the air for plant usage. While the patent holder had created a mixture by selecting and testing for strains of bacteria that did not mutually inhibit one

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analysis of the process claims. Am. Fruit Growers, 283 U.S. at 13-14 ("If it be assumed that the process claims under consideration cover an invention, we think this lacked novelty when application was made for the patent August 13, 1923"). In contrast, its rejection of the composition claims was based on an analysis of subject matter patentability. See id. at 11 ("Is an orange, the rind of which has become impregnated with borax, through immersion in a solution, and thereby resistant to blue mold decay, a 'manufacture,' or manufactured article, within the meaning of section 31, title 35, U.S. Code?").

[42] Myriad suggests that the Supreme Court's holding in Funk Brothers was premised on an obviousness determination, rather than patentable subject matter. Subsequent Supreme Court opinions, however, have treated the holding in Funk Brothers as a statement of patentable subject matter. See Chakrabarty, 447 U.S. at 309-10; Flook, 437 U.S. at 591-92; Benson, 409 U.S. at 67-68.

another, the Court concluded that the patent holder "did not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable." Id. at 130.

Most recently, the Supreme Court addressed the application of § 101 to product claims in Diamond v. Chakrabarty, 447 U.S. 303. In Chakrabarty, the Court considered whether a "live, human-made micro-organism is patentable subject matter under 35 U.S.C. § 101." Id. at 305. The microorganism in question was a bacterium that had been genetically engineered to break down multiple components of crude oil and possessed considerable utility in the treatment of oil spills. Id. In concluding that the man-made bacterial strain was patentable, the Court observed that the claim "is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter - a product of human ingenuity 'having a distinctive name, character [and] use.'" Id. at 309-10 (quoting Hartranft v. Wiegmann, 121 U.S. 609, 615 (1887)). The Court went on to contrast the Chakrabarty bacterium with the bacterial mixture at issue in Funk Brothers, stating that in Chakrabarty's case, "the patentee has produced a new bacterium with markedly

different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own . . . ." Id. at 310.[43] This requirement that an invention possess "markedly different characteristics" for purposes of § 101 reflects the oft-repeated requirement that an invention have "a new or distinctive form, quality, or property" from a product of nature. Am. Fruit Growers, 283 U.S. at 11; In re Merz, 97 F.2d 599, 601 (C.C.P.A. 1935) ("[M]ere purification of known materials does not result in a patentable product," unless "the product obtained in such a case had properties and characteristics which were different in kind from those of the known product rather than in degree.").

Courts have also specifically held that "purification" of a natural compound, without more, is insufficient to render a product of nature patentable. In The American Wood-Paper Co. v. The Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874), the Supreme Court held

[43] Although Chakrabarty is often cited for the proposition that "anything under the sun that is made by man" is patentable, id. at 309, that phrase is a misleading quotation from the legislative history of the Patent Act of 1952. The full quote clearly acknowledges the statutory limitations to patentable subject matter: "A person may have 'invented' a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under section 101 unless the conditions of the title are fulfilled." H.R. Rep. No. 1923, 82d Cong., 2d Sess. 6 (1952).

that refined cellulose, consisting of purified pulp derived from wood and vegetable, was unpatentable because it was "an extract obtained by the decomposition or disintegration of material substance." Id. at 593. As the Court observed:

> There are many things well known and valuable in medicine or in the arts which may be extracted from divers[e] substances. But the extract is the same, no matter from what it has been taken. A process to obtain it from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture.

Id. at 593-94.[44] Similarly, in Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293 (1884), the Court rejected a patent on an artificial version of a natural red dye called alizarine that was produced by manipulating another compound through acid, heat, water or distillation. See generally, id. Although the artificial version of the dye was of a brighter hue than the naturally occurring dye, the Court concluded that "[c]alling it artificial alizarine did not make it a new composition of matter, and patentable as such . . . ." Id. at 311 (citing Am. Wood-Paper, 90 U.S. (23 Wall.) at 593).

[44] Given the posture of the challenge to the patent's validity, the Court rested its holding on the fact that the patent in question was invalid as non-novel. Id.

In General Electric, 28 F.2d at 642, the Third Circuit Court of Appeals considered the patentability of purified tungsten, which possessed superior characteristics and utility over its brittle, naturally-occurring form. The court first noted that "[i]f it is a natural thing then clearly, even if [the patentee] was the first to uncover it and bring it into view, he cannot have a patent for it because a patent cannot be awarded for a discovery or for a product of nature, or for a chemical element." Id. The court went on to state:

> Naturally we inquire who created pure tungsten. Coolidge? No. It existed in nature and doubtless has existed there for centuries. The fact that no one before Coolidge found it there does not negative its origin or existence.
>
> The second part of the claim reads: "Having ductility and high tensile strength." Did Coolidge give those qualities to "substantially pure tungsten"? We think not for it is now conceded that tungsten pure is ductile cold. If it possess that quality now it is certain that it possessed it always.

Id. at 643. The Court of Customs and Patent Appeals ("C.C.P.A."), the precursor to the Federal Circuit Court of

Appeals,[45] subsequently relied on General Electric in rejecting patents claiming purified uranium and vanadium. See In re Marden, 47 F.2d 957, 957-58 (C.C.P.A. 1931) ("Marden I"); In re Marden, 47 F.2d 958, 1059 (C.C.P.A. 1931) ("Marden II") ("The quality of purity of vanadium or its ductility is a quality of a natural product and as such is not patentable."). Similarly, in Ex Parte Latimer, the Patent Commissioner refused to allow a patent on pine needle fibers that were better suited for textile production, even though it was necessary to remove the needle from its sheath and other resinous material. 1889 Dec. Comm'r Pat. 123, 125 (1889) ("Nature made them so and not the process by which they are taken from the leaf or needle.").

Myriad argues that purification of "'naturally occurring' compounds that 'do not exist in nature in pure form' renders such compounds patent-eligible." Myriad Br. at 21 (quoting In re Bergstrom, 427 F.2d 1394, 1401 (C.C.P.A. 1970)). However, Myriad cites no Supreme Court

[45] The decisions of the C.C.P.A. remain binding precedent in patent cases. See South Corp. v. United States, 690 F.2d 1368, 1370-71 (Fed. Cir. 1982) (en banc) (adopting "[t]hat body of law represented by the holdings of . . . the Court of Customs and Patent Appeals" as "precedent" for the then-new Federal Circuit so as to "continu[e] the stability in those areas of the law previously within the jurisdiction of our predecessor courts").

authority that would rebut the authorities presented by Plaintiffs, nor do the cited cases support Myriad's position.

Myriad has relied heavily on the holding of the Honorable Learned Hand in Parke-Davis & Co. v. H.K. Mulford Co., 189 F.2d 95 (S.D.N.Y. 1911).[46] In Parke-Davis, Judge Hand considered a challenge to the validity of a patent

[46] The invocation of Judge Hand is frequently practiced in this Circuit. See, e.g., United States v. Rigas, 583 F.3d 108, 121 n.3 (2d Cir. 2009) (quoting Learned Hand for the proposition that appellate courts may not find facts); United States v. Parker, 554 F.3d 230 (2d Cir. 2009) (quoting Learned Hand for his formulation of the requirements of conspiracy); In re City of New York, 522 F.3d 279, 284 (2d Cir. 2008) (citing Learned Hand for his formulation of negligence); In re Hyman, 501 F.3d 61, 67 (2d Cir. 2007) (quoting at length Learned Hand's inconclusive discussion of the meaning of the word "defalcation" in 11 U.S.C. § 523(a)(4)); United States v. Brand, 467 F.3d 179, 190 (2d Cir. 2006) (quoting Learned Hand's definition of inducement by the government); In re Enron Corp., 419 F.3d 115, 123 (2d Cir. 2005) (quoting Learned Hand's critique of statutes of limitations); Shannon v. Jacobowitz, 394 F.3d 90, 95 (2d Cir. 2005) (quoting Learned Hand's instruction that "[w]ords are not pebbles in alien juxtaposition . . . ."); Danahy v. Buscaglia, 134 F.3d 1185, 1189 (2d Cir. 1998) (quoting Learned Hand on the rationale for qualified immunity). See also, Remarks of the Honorable John M. Walker, Jr. Upon Receiving the Learned Hand Medal for Excellence in Federal Jurisprudence, 76 St. John's L. Rev. 595, 596 (2002) ("Judge Hand is widely considered to have been one of the four greatest judges of the first half of the twentieth century."); James L. Oakes, Personal Reflections on Learned Hand and the Second Circuit, 47 Stan. L. Rev. 387 (1995); Gerald Gunther, Learned Hand: the Man and the Judge (1994); Kathryn Griffin, Judge Learned Hand and the Role of the Federal Judiciary (1973); Marvin Schick, Learned Hand's Court (1970); Marcia Nelson, ed., The Remarkable Hands: An Affectionate Portrait (1983); Hershel Shanks, ed., The Art and Craft of Judging: The Decisions of Judge Learned Hand (1968). Although Judge Hand once turned his back on the author of this opinion arguing before him on behalf of the Government, his opinion in Parke-Davis deserves careful review but brings to mind that oft repeated adage "Quote Learned, but follow Gus." See Oakes, 47 Stan. L. Rev. at 389 n.175. This author, confronted by genomics and molecular biology, also emphatically empathizes with Judge Hand's complaint in Parke-Davis about his lack of knowledge of the rudiments of chemistry. See Parke-Davis, 189 F. at 114.

claiming an adrenaline compound that had been isolated and purified from animal suprarenal glands. Id. at 97. It had been known that suprarenal glands in powdered form had hemostatic, blood-pressure-raising and astringent properties, but could not be used for those purposes in gross form. The isolated adrenaline, however, possessed the desired therapeutic properties and could be administered to humans.

Although Myriad argues that the holding in Parke-Davis establishes that the purification of a natural product necessarily renders it patentable, the opinion, read closely, fails to support such a conclusion. The question before the court in Parke-Davis was one of novelty (a modern-day § 102 question), not of patentable subject matter (the § 101 question before this Court). In framing the issue, Judge Hand observed that, "[the validity of the claims] is attacked, first, because they are *anticipated* in the art; and second, for a number of technical grounds which I shall take up in turn." Id. at 101 (emphasis added). He went on to conclude that the patented purified extract was not, in fact, different from the prior art "only for a degree of purity," but rather was a different chemical substance from that found in the prior art. Id.

at 103 (observing that "no one had ever isolated a substance [adrenaline] which was not in salt form" and that "the [claimed] base [form of adrenaline] was an original production of [the patentee's]"). Thus, Judge Hand held that the purified adrenaline was not anticipated by the prior art, namely, the ground paradrenal gland that was known to possess certain beneficial properties. See Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 162 (4th Cir. 1958) ("It was further held [in Parke-Davis] that the invention was not anticipated, though the principle was known to exist in the suprarenal glands.").

Only after concluding that the claimed purified adrenaline was novel over the prior art did Judge Hand offer, as dicta, the statement to which Myriad cites: "But, even if it were merely an extracted product without change, there is no rule that such products are not patentable." Id. at 103. While the accuracy of this statement at the time was written is dubious in light of American Wood-Paper (to which Judge Hand did not cite) it is certainly no longer good law in light of subsequent Supreme Court cases, which, as noted above, require that a claimed invention possess "markedly different characteristics" over products existing in nature in order for it to constitute patentable

subject matter.[47] Chakrabarty, 447 U.S. at 310; see also Funk Bros., 333 U.S. at 130-32. By the same token, Judge Hand's suggestion that a claimed invention was patentable since it was a "new thing commercially and therapeutically," Parke-Davis, 189 F.2d at 103, is firmly contradicted by subsequent case law establishing that "it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements" when evaluating whether a claim is patent-eligible subject matter. Prometheus, 581 F.3d at 1343; see also Bergy, 596 F.2d at 960-61. Such an approach would also be inconsistent with the Supreme Court's rejection of the patentability of the commercially useful mixture of bacteria in Funk Brothers, the refined cellulose in American Wood-Paper, and the electromagnetic communication devices in O'Reilly v. Morse, 56 U.S. (15 How.) 62 (1853).

The distinction between considerations of novelty and patentable subject matter similarly undermines Myriad's reliance on Bergstrom and In re Kratz, 592 F.2d 1169 (C.C.P.A. 1979), both of which presented issues of novelty

[47] Notwithstanding Judge Hand's reputation, see supra note 46, his opinion in Parke-Davis was one of a district court judge and does not supersede contrary statements of the law by the C.C.P.A. or the Supreme Court.

and anticipation rather than the question of patentable subject matter. In Bergstrom, the C.C.P.A. considered an appeal from a rejection by the Board of Patent and Interferences ("BPAI") of a patent claiming the purified prostaglandins PGE_2 and PGE_3 that had been extracted from human or animal prostate glands. 427 F.2d at 1398. Although the BPAI cited § 101 in its rejection, the C.C.P.A. recognized the issue as a § 102 question of novelty. Id. at 1400 ("Tested by the conventional evidentiary criteria or 'conditions for patentability' relevant to the present factual situation which Congress has expressed in the various provisions of 35 U.S.C. § 102, appellants are undoubtedly correct, for the Patent Office has not been able to . . . establish that the claimed subject matter lacks 'novelty.'"); see also id. at 1401 ("[T]he fundamental error in the board's position, as we see it, is the analysis and answer it gave to the sole issue it accurately posed - whether the claimed pure materials are novel as compared with the less pure materials of the reference." (internal citation and quotation marks omitted)). Indeed, the C.C.P.A. itself has subsequently recognized that Bergstrom is properly viewed as a case concerning novelty. Bergy, 596 F.2d at 961 ("Our research has disclosed only two instances in which

rejections for lack of novelty were made by the PTO under § 101 . . . . In In re Bergstrom we in effect treated the rejection as if it had been made under § 102, observing in the process that 'The word "new" in § 101 is defined and to be construed in accordance with the provisions of § 102.'" (internal citation omitted)).

Kratz examined the rejection of a patent claiming a substantially purified chemical compound naturally occurring in strawberries, called 2-methyl-2-pentenoic acid ("2M2PA"). 592 F.2d at 1170. The patentee had appealed from the BPAI's determination that the purified compound was obvious over the prior art under § 103. See id. Although there was some discussion about whether the composition claimed was a naturally-occurring compound, the C.C.P.A. did not view the question before it as a § 101 inquiry. Instead, the court treated the appeal as a question of novelty and anticipation pursuant to § 102.[48] See, e.g., id. at 1174 ("It should be clear that an

[48] The differences between the test applied in Kratz and the "markedly different" requirement set forth in Chakrabarty and other Supreme Court precedent further demonstrates that the Kratz court was engaged in a § 102 anticipation analysis and not a § 101 statutory subject matter analysis. See id. at 1174 (requiring, for a finding of anticipation, that "the natural composition must inherently contain the naturally occurring compound" and that "the claim must be of sufficient breadth to encompass both the known natural composition and the naturally occurring compound.").

anticipation rejection in such a case is necessarily based on a dual footing.").[49]

Finally, Merck & Co., Inc. v. Olin Mathieson Chem. Corp., 253 F.2d 156, cited by Myriad, is entirely consistent with the principle set forth in Funk Brothers and American Fruit Growers that something derived from a product of nature must "possess a new or distinctive form, quality, or property" in order to become patentable subject matter. Am. Fruit Growers, 283 U.S. at 11. In Merck, the Fourth Circuit considered the validity of a patent claiming a Vitamin B_{12} composition useful for treating pernicious anemia. Id. at 157. Although naturally occurring Vitamin B_{12} produced in cows had known therapeutic properties and was commercially available, the court found the purified B_{12} composition, which was obtained from a microorganism, patentable. In upholding the validity of the patent, the court held:

> Every slight step in purification does not produce a new product. What is gained may be the

[49] Bergy, also cited by Myriad, considered the question of whether microorganisms constituted patentable subject matter, an issue subsequently addressed by the Supreme Court in Chakrabarty. It did not address the patentability of purified natural products, and its citation to Merck and Parke-Davis was only for the purpose of noting that courts had upheld patents on pharmaceutical compounds such as vitamin B_{12} and adrenaline. See Bergy, 596 F.2d at 974-75 & n.13.

> old product, but with a greater degree of purity. Alpha alumina purified is still alpha alumina, In re Ridgway, 76 F.2d 602,[] and ultramarine from which floatable impurities have been removed is still ultramarine, In re Merz, 97 F.2d 599 . . . .

Id. at 163. Because the court concluded that the purified B_{12} was more than a "mere advance in the degree of purity of a known product," it determined that the claimed invention was entitled to patent protection. Id. at 164.

In sum, the clear line of Supreme Court precedent and accompanying lower court authorities, stretching from American Wood-Paper through to Chakrabarty, establishes that purification of a product of nature, without more, cannot transform it into patentable subject matter. Rather, the purified product must possess "markedly different characteristics" in order to satisfy the requirements of § 101.

3. The claimed isolated DNA is not "markedly different" from native DNA

The question thus presented by Plaintiffs' challenge to the composition claims is whether the isolated DNA claimed by Myriad possesses "markedly different

characteristics" from a product of nature.[50] Chakrabarty, 447 U.S. at 310. In support of its position, Myriad cites several differences between the isolated DNA claimed in the patents and the native DNA found within human cells. None, however, establish the subject matter patentability of isolated *BRCA1/2* DNA.

The central premise of Myriad's argument that the claimed DNA is "markedly different" from DNA found in nature is the assertion that "[i]solated DNA molecules should be treated no differently than other chemical compounds for patent eligibility," Myriad Br. at 26, and that the alleged "difference in the structural and functional properties of isolated DNA" render the claimed DNA patentable subject matter, Myriad Br. at 31.

Myriad's focus on the chemical nature of DNA, however, fails to acknowledge the unique characteristics of DNA that differentiate it from other chemical compounds. As Myriad's expert Dr. Joseph Straus observed: "Genes are of double nature: On the one hand, they are chemical substances or molecules. On the other hand, they are

[50] The parties do not appear to dispute that isolated DNA claimed in the patents-in-suit are "useful" for purposes of § 101.

physical carriers of information, i.e., where the actual biological function of this information is coding for proteins. Thus, inherently genes are multifunctional." Straus Decl. ¶ 20; see also *The Cell* at 98, 104 ("Today the idea that DNA carries genetic information in its long chain of nucleotides is so fundamental to biological thought that it is sometimes difficult to realize the enormous intellectual gap that it filled. . . . DNA is relatively inert chemically."); Kevin Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* 166 (1996) (noting that Myriad Genetics' April 1994 press release described itself as a "genetic information business"). This informational quality is unique among the chemical compounds found in our bodies, and it would be erroneous to view DNA as "no different[]" than other chemicals previously the subject of patents.[51]

[51] Myriad and many of the amici suggest that the invalidation of the patents-in-suit will result in the decimation of the biotechnology industry. See, e.g., Myriad Br. at 28-29 (suggesting that a finding that DNA is unpatentable subject matter will invalidate patents to important chemical compounds such as the anticancer drug Taxol (paclitaxel) and leave "little to nothing" of the United States biotechnology industry). The conclusions reached in this opinion concerning the subject matter patentability of isolated DNA, however, are based on the unique properties of DNA that distinguish it from all other chemicals and biological molecules found in nature. As a result, Myriad's predictions for the future of the U.S. biotechnology industry are unfounded.

Myriad's argument that all chemical compounds, such as the adrenaline at issue in Parke-Davis, necessarily conveys some information ignores the biological realities of DNA in comparison to other chemical compounds in the body. The information encoded in DNA is not information about its *own* molecular structure incidental to its biological function, as is the case with adrenaline or other chemicals found in the body. Rather, the information encoded by DNA reflects its primary biological function: directing the synthesis of *other* molecules in the body - namely, proteins, "biological molecules of enormous importance" which "catalyze biochemical reactions" and constitute the "major structural materials of the animal body." O'Farrell, 854 F.2d at 895-96. DNA, and in particular the ordering of its nucleotides, therefore serves as the physical embodiment of laws of nature - those that define the construction of the human body. Any "information" that may be embodied by adrenaline and similar molecules serves no comparable function, and none of the declarations submitted by Myriad support such a conclusion. Consequently, the use of simple analogies comparing DNA with chemical compounds previously the subject of patents cannot replace consideration of the distinctive characteristics of DNA.

In light of DNA's unique qualities as a physical embodiment of information, none of the structural and functional differences cited by Myriad between native *BRCA1/2* DNA and the isolated *BRCA1/2* DNA claimed in the patents-in-suit render the claimed DNA "markedly different." This conclusion is driven by the overriding importance of DNA's nucleotide sequence to both its natural biological function as well as the utility associated with DNA in its isolated form. The preservation of this defining characteristic of DNA in its native and isolated forms mandates the conclusion that the challenged composition claims are directed to unpatentable products of nature.

Myriad argues that the § 101 inquiry into the subject matter patentability of isolated DNA should focus exclusively on the differences alleged to exist between native and isolated DNA, rather than considering the similarities that exist between the two forms of DNA. See, e.g., Myriad Reply at 8-9 ("[T]he observation that isolated DNA and native DNA share this single property [i.e. the same protein coding sequences] is irrelevant to the critical issue of whether there are *differences* in their

properties. It is the *differences* that are legally relevant to the novelty inquiry under Section 101, not the properties held in common." (emphasis in original)); Myriad Br. at 8. Setting aside the fact that considerations such as novelty are irrelevant for § 101 purposes, see Bergy, 596 F.2d at 960-61, Myriad offers no authorities supporting such an approach. To the contrary, the Supreme Court has held that "[i]n determining the eligibility of [a] claimed process for patent protection under § 101, [the] claims must be considered as a whole." Diehr, 450 U.S. at 188. Similarly, the Federal Circuit has expressly held that "[i]n the final analysis under § 101, the claimed invention, as a whole, must be evaluated for what it is." In re Grams, 888 F.2d 835, 839 (Fed. Cir. 1989) (quoting In re Abele, 684 F.2d 902, 907 (C.C.P.A. 1982)).

Were Myriad's approach the law, it is difficult to discern how any invention could fail the test. For example, the bacterial mixture in Funk Brothers was unquestionably different from any preexisting bacterial mixture; yet the Supreme Court recognized that a patent directed to the mixture, considered as a whole, did no more than patent "the handiwork of nature." 333 U.S. at 131. There will almost inevitably be some identifiable

differences between a claimed invention and a product of nature; the appropriate § 101 inquiry is whether, considering the claimed invention as a whole, it is sufficiently distinct in its fundamental characteristics from natural phenomena to possess the required "distinctive name, character, [and] use." Chakrabarty, 447 U.S. at 309-10.

None of Myriad's arguments establish the distinctive nature of the claimed DNA. Myriad's argument that association of chromosomal proteins with native DNA establishes the existence of "structural differences" between native and isolated DNA relies on an incorrect comparison between isolated DNA and *chromatin*, which are indeed different insofar as chromatin includes chromosomal proteins normally associated with DNA. The proper comparison is between the claimed isolated DNA and the corresponding native DNA, and the presence or absence of chromosomal proteins merely constitutes a difference in purity that cannot serve to establish subject matter patentability. See Gen. Elec., 28 F.2d at 642-43; Marden I, 47 F.2d at 957-58; Marden II, 47 F.2d at 1059.

Myriad also attempts to rely on its assertion that native DNA contains intron sequences that are absent in the claimed *BRCA1/2* DNA. However, some of the claims, such as claim 1 of the '282 patent, are directed broadly to DNA "coding for a BRCA1 polypeptide." Native *BRCA1* DNA, by definition, encodes the BRCA1 protein; thus claim 1 of the '282 patent would cover purified *BRCA1* DNA possessing the exact same structure found in the human cell, introns and all.[52] See also '492 patent, claim 1 (similarly claiming isolated DNA "coding for a BRCA2 polypeptide"). In addition, several of the composition claims are directed to isolated DNA containing as few as 15 nucleotides of the *BRCA1* coding sequence, see, e.g., '282 patent, claims 5 & 6, and at least some of these short DNA sequences will be found within a single exon of the native *BRCA1* gene sequence. See Adam Pavlicek, et al., Evolution of the Tumor Suppressor *BRCA1* Locus in Primates: Implications for Cancer Predisposition, 13 Human Molecular Genetics 2737, 2737 (2004) (noting *BRCA1* exons range from 37 to 3427 nucleotides in length). Therefore, for these small DNA fragments, the existence of introns in native *BRCA1* DNA is completely irrelevant to the question of structural

[52] To the extent a claim reads on unpatentable subject matter, the entire claim must be deemed invalid. See Titanium Metals Corp. of Am. v. Banner, 778 F.2d 775, 782 (Fed. Cir. 1985).

differences when comparing these short DNA molecules with native *BRCA1* DNA.

More generally, the fact that the *BRCA1/2* cDNA molecules covered by the composition claims-in-suit contain only the protein coding exons and not the introns found in native DNA does not render these cDNAs and their native counterparts "markedly different." The splice variants represented by these cDNAs are the result of the naturally-occurring splicing of pre-mRNA into mature mRNA. Therefore, not only are the coding sequences contained in the claimed DNA identical to those found in native DNA, the particular arrangement of those coding sequences is the result of the natural phenomena of RNA splicing. Finally, at least in the case of *BRCA1*, the claimed cDNA sequences are actually found in the human genome in the form of a naturally occurring pseudogene. See Mason Supp. Decl. ¶ 18.[53]

[53] Native DNA is sometimes methylated, but that methylation is preserved when the DNA is extracted and purified. Nussbaum Decl. ¶ 20. Since the claimed "isolated DNA" includes DNA extracted and purified from the body, methylation of DNA in the body does not distinguish native DNA from the claimed DNA. In addition, DNA in the body also exists in a non-methylated state, just as the synthesized DNA claimed in the patents would not be methylated. More importantly, while methylation affects the transcription of a gene in the body, it does not have any impact on the genetic information contained within the DNA. Indeed, DNA is demethylated and remethylated as it passes from the germline of one generation to the next. Nussbaum Decl. ¶ 28.

Myriad's argument that the functional differences between native and isolated DNA demonstrates that they are "markedly different" relies on the fact that isolated DNA may be used in applications for which native DNA is unsuitable, namely, in "molecular diagnostic tests (e.g., as probes, primers, templates for sequencing reactions), in biotechnological processes (e.g. production of pure *BRCA1* and *BRCA2* protein), and even in medical treatments (e.g. gene therapy)." Myriad Reply at 9; see also Myriad Br. at 30-32.

Isolated DNA's utility as a primer or a molecular probe (for example, for Southern blots) arises from its ability to "target and interact with other DNA molecules," that is, the ability of a given DNA molecule to bind exclusively to a specific DNA target sequence. Myriad Br. at 33; see Kay Decl. ¶ 138. Thus, for example, a 24 nucleotide segment of isolated *BRCA1* DNA can be used as a primer because it will bind only to its corresponding location in the *BRCA1* gene. However, the basis for this utility is the fact that the isolated DNA possesses the identical nucleotide sequence as the target DNA sequence,[54]

[54] To be precise, the isolated single-stranded DNA molecule utilized as a primer or probe has the identical sequence as the complementary DNA strand to the DNA strand containing the target DNA sequence. The

thus allowing target specific hybridization between the DNA primer and the portion of the target DNA molecule possessing the corresponding sequence. Kay Decl. ¶¶ 135-36, 138. In contrast, another 24 nucleotide segment of DNA possessing the same nucleotide composition but a different nucleotide sequence would not have the same utility because it would be unable to hybridize to the proper location in the *BRCA1* gene.[55] Indeed, Myriad implicitly acknowledges this fact when it states that the usefulness of isolated DNA molecules "is based on their ability to target and interact with other DNA molecules, which is a function of *their own individual structure and chemistry*." Myriad Br. at 33 (emphasis added). Therefore, the cited utility of the isolated DNA as a primer or probe is primarily a function of the nucleotide sequence identity between native and isolated *BRCA1/2* DNA.

Similarly, the utility of isolated DNA as a sequencing target relies on the preservation of native DNA's nucleotide sequence. Indeed, one need look no further than Myriad's BRACAnalysis testing, which relies on the sequencing of isolated DNA (i.e. the PCR amplified

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description in the text is meant to serve as a short-hand description of this relationship.

[55] The same reasoning applies with respect to the use of isolated DNA as a probe. See Kay Decl. ¶¶ 135-36.

exons of *BRCA1/2*), to determine the sequence of the corresponding DNA coding sequences found in the cell. The entire premise behind Myriad's genetic testing is that the claimed isolated DNA retains, in all relevant respects, the identical nucleotide sequence found in native DNA. The use of isolated *BRCA1/2* DNA in the production of BRCA1/2 proteins or in gene therapy also relies on the identity between the native DNA sequences and the sequences contained in the isolated DNA molecule. Were the isolated *BRCA1/2* sequences different in any significant way, the entire point of their use - the production of BRCA1/2 proteins - would be undermined.

While the absence of proteins and other nucleotide sequences is currently required for DNA to be useful for the cited purposes, the purification of native DNA does not alter its essential characteristic - its nucleotide sequence - that is defined by nature and central to both its biological function within the cell and its utility as a research tool in the lab. The requirement that the DNA used be "isolated" is ultimately a technological limitation to the use of DNA in this fashion, and a time may come when the use of DNA for molecular and diagnostic purposes may not require such purification. The

nucleotide sequence, however, is the defining characteristic of the isolated DNA that will always be required to provide the sequence-specific targeting and protein coding ability that allows isolated DNA to be used for the various applications cited by Myriad. For these reasons, the use of isolated DNA for the various purposes cited by Myriad does not establish the existence of differences "in kind" between native and isolated DNA that would establish the subject matter patentability of what is otherwise a product of nature. See Am. Fruit Growers, 283 U.S. at 11.

Finally, the isolated *BRCA1/2* DNA claimed in Myriad's patents bears comparison to the bacterial mixture in Funk Brothers. In explaining why the claimed mixture of bacteria did not constitute an invention, the Court observed that the first part of the claimed invention was the "[d]iscovery of the fact that certain strains of each species of these bacteria can be mixed without harmful effect to the properties of either" which was "a discovery of their qualities of non-inhibition. It is no more than the discovery of some of the handiwork of nature and hence is not patentable." 33 U.S. at 131. The Court went on to observe that the second part of the claimed invention was

"[t]he aggregation of select strains of the several species into one product[,] an application of that newly-discovered natural principle. But however ingenious the discovery of that natural principle may have been, the application of it is hardly more than an advance in the packaging of the inoculants." Id.

According to Myriad, the invention claimed in its patents required the identification of the specific segments of chromosomes 17 and 13 that correlated with breast and ovarian cancer (*BRCA1* and *BRCA2*) followed by the isolation of these sequences away from other genomic DNA and cellular components. Myriad Reply at 6 ("By identifying these particular *BRCA* DNAs and isolating them away from other genomic DNA and other cellular components, the inventors created the claimed isolated *BRCA* DNA molecules."). Like the discovery of the mutual non-inhibition of the bacteria in Funk Brothers, discovery of this important correlation was a discovery of the handiwork of nature - the natural effect of certain mutations in a particular segment of the human genome. And like the aggregation of bacteria in Funk Brothers, the isolation of the *BRCA1* and *BRCA2* DNA, while requiring technical skill and considerable labor, was simply the application of

techniques well-known to those skilled in the art. See Parthasarathy Decl. ¶ 19. The identification of the *BRCA1* and *BRCA2* gene sequences is unquestionably a valuable scientific achievement for which Myriad deserves recognition, but that is not the same as concluding that it is something for which they are entitled to a patent. See Funk Bros., 33 U.S. at 132 ("[O]nce nature's secret of the non-inhibitive quality of certain strains of the [nitrogen-fixing bacteria] was discovered, the state of the art made the production of a mixed inoculant a simple step. Even though it may have been the product of skill, it certainly was not the product of invention.").

Because the claimed isolated DNA is not markedly different from native DNA as it exists in nature, it constitutes unpatentable subject matter under 35 U.S.C. § 101.

D. The Method Claims are Invalid Under 35 U.S.C. § 101

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." Benson, 409 U.S. at 67. However,

"'an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.'" Bilski, 545 F.3d at 953 (quoting Diehr, 450 U.S. at 187). In Bilski, the Federal Circuit set forth "the definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than pre-empt the principle itself." Id. at 954. Under this "machine or transformation" test, "[a] claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." Id. In addition, "the use of a specific machine or transformation of an article must impose meaningful limits on the claim's scope to impart patent-eligibility," and "the involvement of the machine or transformation in the claimed process must not merely be insignificant extra-solution activity." Id. at 961-62. In other words, the "transformation must be central to the purpose of the claimed process." Id. at 962. In particular, the Bilski court held that "adding a data-gathering step to an algorithm is insufficient to convert that algorithm into a patent-eligible process." Id. at 963 (citing Grams, 888 F.2d at 840; Meyer, 688 F.2d at 794). "A requirement

simply that data inputs be gathered - without specifying how - is a meaningless limit on a claim to an algorithm because every algorithm inherently require the gathering of data inputs." Id. (citing Grams, 888 F.2d at 839-40). "Further, the inherent step of gathering data can also fairly be characterized as insignificant extra-solution activity." Id. (citing Flook, 437 U.S. at 590).

1. The claims for "analyzing" and "comparing" DNA sequences are invalid under § 101

Claim 1 of the '999 patent is directed to the process of "analyzing" a *BRCA1* sequence and noting whether or not the specified naturally-occurring mutations exist. The claimed process is not limited to any particular method of analysis and does not specify any further action beyond the act of "analyzing." Similarly, claim 1 of the '001, '441, and '857 patents as well as claim 2 of the '857 patents are directed to "comparing" two gene sequences to see if any differences exist and do not specify any limitations on the method of comparison.

Myriad argues that these method claims should not be viewed as mental processes because they incorporate a

transformation step and therefore satisfy the "transformation" prong of the Bilski "machine or transformation" test. In support of its position, Myriad relies primarily on the Federal Circuit's holding in Prometheus, 581 F.3d 1336. There, the Federal Circuit considered a patent containing claims directed to methods for calibrating the proper dosage of thiopurine drugs by measuring metabolites in subjects having gastrointestinal disorders. Id. at 1343-50. The patentees had discovered a correlation between metabolite levels in a patient's blood and the therapeutic efficacy of a dose of the drug. Based on this correlation, the patentees claimed methods to optimize therapeutic efficiency while minimizing side effects by determining metabolite levels and identifying a need to adjust drug dosage upward or downward based on the levels. Id. at 1339-40. A representative claim asserted by the patentee in Prometheus claimed:

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

> wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and
>
> wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Id. at 1340.

In concluding that the claimed methods satisfied the requirements of § 101, the Federal Circuit held that the relevant transformation for purposes of the "machine or transformation" test was the transformation of the human body as well as the chemical and physical changes of the drug's metabolites. Id. at 1346 (stating that "claims to methods of treatment," were "always transformative when a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition"). Because the transformative steps were central to the claimed treatment methods, they satisfied the "machine or transformation" test. Id. at 1346-47. The court went on to hold that the "determining" step alone was transformative and central to the claimed methods since "determining the levels of [the metabolites] 6-TG or 6-MMP

in a subject necessarily involves a transformation, for those levels cannot be determined by mere inspection." Id. at 1347.

Myriad argues that just as the act of "determining" metabolite levels in Prometheus was found to involve the transformation of human blood, so too should "analyzing" or "comparing" *BRCA1/2* gene sequences be construed to incorporate physically transformative steps (i.e. the isolation and sequencing of DNA[56]) that would satisfy the Bilski "machine or transformation" test. Myriad further asserts that these transformations are "central to the purpose of the claims," id. at 1347, because "Myriad's method claims each require the transformation of a tissue or blood sample in order to isolate the patient's DNA." Myriad Br. at 35.

The claims in Prometheus, however, are distinguishable from the method claims in dispute here. In Prometheus, "determining metabolite levels in the clinical samples taken from patients" was found to be transformative because the act of "determining metabolite levels" was

[56] The challenged method claims are also directed to analyzing and comparing RNA and cDNA sequences, but for purposes of this opinion, the discussion will be framed in terms of analyzing and comparing DNA sequences.

itself construed to include the extraction and measurement of metabolite concentrations, such as high pressure liquid chromatography. See Prometheus, 581 F.3d at 1347. Indeed, neither party in Prometheus disputed that "determining" metabolite levels in samples taken from patients was, in and of itself, transformative.[57] Id.

In contrast, the language of the method claims-in-suit and the plain and ordinary meanings of the terms "analyzing" or "comparing" establish that the method claims-in-suit are directed only to the abstract mental processes of "comparing" or "analyzing" gene sequences. Although Myriad asserts that the challenged method claims are directed to comparing DNA molecules rather than DNA sequences, the language of the claims belies such an interpretation. While the *purpose* of the claimed method is, for example, to "detect a germline alteration in a BRCA1 gene," see '999 patent, col. 161:17-18, the *method* actually claimed is "analyzing a *sequence* of a BRCA1 gene." '999 patent, col. 161: 20-21 (emphasis added); see also '001 patent, col. 144:2-17 ("A method . . . which comprises gene comparing a first sequence selected from the group

[57] The issue with respect to the "determining" step was not whether it was transformative, but whether that transformation was central to the claimed invention. Id.

consisting of a BRCA1 gene from said tumor sample . . . with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample . . . wherein a difference in the sequence of the BRCA1 gene . . . indicates a somatic alteration in the BRCA1 gene."); '857 patent, col. 169:40-45 ("A method . . . which comprises comparing the nucleotide sequence of the suspected mutant BRCA2 allele with the wild-type BRCA2 nucleotide sequence . . . .").

Similarly, the inclusion of the phrases "from a human subject" or "from a nontumor sample" in the claims serve only to specify the identity of the DNA or RNA sequence to be "analyzed" or "compared," i.e., from a human sample as opposed to an animal sample or cell culture, and do not, as Myriad argues, establish that the claims should be read to include the physical transformations associated with obtaining DNA from those sources.[58] In addition, the

[58] Whether acts are "transformative" in the context of the "machine or transformation" test for process claims is distinct from the question of whether those acts would render the resulting product patentable subject matter. See, e.g., Am. Wood-Paper, 90 U.S. (23 Wall.) at 593-94 (noting that a party may be entitled to a patent on a process for purifying a natural product but not the final product itself if the final product is not different "in kind" from the natural product); Merz, 97 F.2d at 601 (same). Therefore the description of DNA purification and sequencing as "transformative acts" in the context of the challenged process claims is not inconsistent with the conclusion that the isolated DNAs claimed in the challenged patents constitute unpatentable subject matter.

passages from the '999 specification cited by Myriad describing the process by which DNA sequences are obtained cannot serve to redefine the scope of the challenged claims without violating the prohibition against importing claim limitations from the specification. See Phillips, 415 F.3d at 1320.

By the same token, the transformative steps associated with isolating and sequencing DNA described in the unchallenged dependent claims cannot be used to establish that the challenged claims include transformative events. To do so would violate the doctrine of claim differentiation, which presumes that "different words or phrases used in separate claims . . . indicate that the claims have different meanings and scope." Karlin Tech., Inc. v. Surgical Dynamics, Inc., 177 F.3d 968, 972 (Fed. Cir. 1999). Because claim differentiation "prevents the narrowing of broad claims by reading into them the limitations of narrower claims," Clearstream Wastewater Sys., Inc. v. Hydro-Action, Inc., 206 F.3d 1440, 1446 (Fed. Cir. 2000), the dependent claims serve only to illustrate the breadth of the challenged claims and reinforce the conclusion that what is claimed are mental processes independent of any physical transformations. See Phillips,

415 F.3d at 1314-15 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim.").[59]

Myriad also argues that because isolating and sequencing DNA are required for "analyzing" or "comparing" DNA sequences, Prometheus allows those transformative acts to be incorporated into the process claims for purposes of the § 101 analysis. See Myriad Reply at 12. Myriad thus seeks to rely on transformations not actually claimed by the method claims-in-suit to satisfy the Bilski "machine or transformation" test. Neither Prometheus nor any other authority supports such an expansive approach to the application of this test. Prometheus held only that the term "determining," as used in the claims at issue, referred to acts that included manipulations that satisfied the "machine or transformation" test. Id. Nowhere did Prometheus suggest that preparatory physical transformations required for the performance of, but not included in, claims directed to mental processes should be

[59] The patent examiner's reasons for allowance, cited by Myriad, are precisely the legal conclusions concerning the patentability of the claimed methods being challenged by Plaintiffs. Moreover, the examiner's reasons of allowance cannot serve to define the scope of claim terms. See ACCO Brands, Inc. v. Micro Sec. Devices, Inc., 346 F.3d 1075, 1079 (Fed. Cir. 2003).

incorporated into the claim for purposes of the § 101 analysis. Not only would such an approach be inconsistent with the prohibition on the importation of claim limitations from the specification, it would effectively vitiate the limitations to claiming mental processes provided by the "machine or transformation" test since "to use virtually any natural phenomenon for virtually any useful purpose could well involve the use of empirical information obtained through an unpatented means that might have involved transforming matter." Metabolite Labs., 548 U.S. at 136 (Breyer, J., dissenting). Therefore the preparatory transformations relating to obtaining DNA sequences cannot be relied on to satisfy the requirements of § 101.

Even if the challenged method claims were read to include the transformations associated with isolating and sequencing human DNA, these transformations would constitute no more than "data-gathering step[s]" that are not "central to the purpose of the claimed process." Bilski, 545 F.3d at 962-63. In Grams, the Federal Circuit considered a patent directed to a method of diagnosing an abnormal condition in an individual. The claimed method consisted of two steps: (1) "performance of clinical

laboratory tests on an individual to obtain data for the parameters," and (2) "analyz[ing] that data to ascertain the existence and identity of an abnormality . . . ." 888 F.2d at 837. Concluding that the essence of what was claimed was the mathematical algorithm for analyzing the clinical data, and that the sole physical process - laboratory testing - was merely data-gathering to obtain clinical data, the court held the patent invalid under § 101 for claiming a mathematic algorithm. Id. at 840.

The method claims-in-suit present a closely analogous situation. The essence of what is claimed is the identification of a predisposition to breast cancer based on "analyzing" or "comparing" *BRCA1/2* gene sequences. See, e.g., '857 patent, claim 2 ("A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the [BRCA2 gene sequence] from said subject with the [] sequence of the wild-type BRCA2 gene . . . ."). As in Grams, isolation and sequencing of DNA from a human sample, even if incorporated into the method claims-in-suit, would represent nothing more than data-gathering steps to obtain the DNA sequence information on which to perform the claimed comparison or analysis. Moreover, in the absence of a specified method for

isolating and sequencing DNA, "[a] requirement simply that data inputs be gathered - without specifying how - is a meaningless limit on a claim to an algorithm because every algorithm inherently requires the gathering of data inputs." Bilski, 545 F.3d at 963 (citing Grams, 888 F.2d at 839-40). Consequently, even if the method claims-in-suit were construed to include the physical transformations associated with isolating and sequencing DNA, they would still fail the "machine or transformation" test under § 101 for subject matter patentability.

2. The claim for "comparing" the growth rate of cells is invalid under § 101.

Claim 20 of the '282 patent is directed to "comparing" the growth rates of cells in the presence or absence of a potential cancer therapeutic. Specifically, the claim recites a method for identifying potential cancer therapeutics by utilizing cells into which an altered *BRCA1* gene known to cause cancer has been inserted. Thus modified to mimic cancerous cells in the body, these cells are then grown in either the presence or absence of a potential cancer therapeutic, and the growth rates of the

cells are compared to determine the effect of the potential therapeutic.

Unlike the method claims directed to "analyzing" or "comparing" DNA sequences, claim 20 arguably recites certain transformative steps, such as the administration of the test compound.[60] However, the essence of the claim, when considered in its entirety, is the act of comparing cell growth rates and concluding that "a slower growth of said host cell in the presence of said compound is indicative of a cancer therapeutic." '282 patent, col. 156:25-27.

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[60] It is questionable whether the two transformations cited by Myriad are relevant transformations for purposes of the § 101 inquiry. Under Prometheus, the administration of a test compound is transformative only if it effects a change in cell growth. See Prometheus, 581 F.3d at 1346 (finding "administering" of a drug transformative since it resulted in changes to both the patient and the drug metabolites). If the test compound had no effect on the cells, it is unclear whether there would be any basis to view its administration as working a "transformation" since there would be no transformation with respect to the cells (i.e. there was no change in their growth rate) and there would also presumably be no transformation with respect to the test drug (i.e. it was not metabolized).

The other alleged "transformation" cited by Myriad is the insertion of DNA into cells to create the "transformed eukaryotic cell" for treatment with the test compound. Kay Decl. ¶ 57. Even more that its expansive interpretation of the method claims for analyzing DNA sequences for § 101 purposes, Myriad's attempt to rely on transformations associated with the creation of a starting product for its claimed process is unsupported by the law and demonstrates the limitlessness of Myriad's interpretation of Prometheus and the "machine or transformation" test.

This claimed "process" is, in fact, the scientific method itself, and claim 20 seeks to patent a basic scientific principle: that a slower rate of cell growth in the presence of a compound indicates that the compound may be a cancer therapeutic. The recited transformative steps, as in Grams, represent nothing more than preparatory, data-gathering steps to obtain growth rate information and do not render the claimed mental process patentable under § 101. See Grams, 888 F.2d at 840 ("The presence of a physical step in the claim to derive data for the algorithm will not render the claim statutory").[61]

E. The Constitutional Claims Against the USPTO Are Dismissed

As determined above, the patents issued by the USPTO are directed to a law of nature and were therefore improperly granted. The doctrine of constitutional avoidance, which states that courts should not reach unnecessary constitutional questions, thereby becomes applicable. See, e.g., Allstate Ins. Co. v. Serio, 261 F.3d 143, 149-50 (2d Cir. 2001) ("It is axiomatic that the

[61] Because Plaintiffs' motion for summary judgment with respect to its claims against Myriad is granted on the basis of 35 U.S.C. § 101, its Constitutional claims need not be addressed.

federal courts should, where possible, avoid reaching constitutional questions.") (citing Spector Motor Serv., Inc. v. McLaughlin, 323 U.S. 101 (1944) ("If there is one doctrine more deeply rooted than any other in the process of constitutional adjudication, it is that we ought not to pass on questions of constitutionality . . . unless such adjudication is unavoidable")); see also Ashwander v. TVA, 297 U.S. 288, 347 (1936) (Brandeis, J., concurring) ("[I]f a case can be decided on either of two grounds, one involving a constitutional question, the other a question of statutory construction or general law, the Court will decide only the latter."). This doctrine bears on the consideration of Plaintiffs' claims that the USPTO's policy permitting the grant of the Myriad patents violates Article I, Section 8, Clause 8 and the First Amendment of the Constitution.

The Plaintiffs have not addressed these authorities and have contended that "the doctrine of constitutional avoidance is inapplicable" because the invalidation of Myriad's claims pursuant to 35 U.S.C. § 101 "will not necessarily invalidate the USPTO's policy [in granting the patents]." Pl. Reply at 43. However, a decision by the Federal Circuit or the Supreme Court

affirming the holding set forth above would apply to both the issued patents as well as patent applications and would be binding on all patent holders and applicants, as well as the USPTO. See Koninklijke Philips Electronics N.V. v. Cardiac Science, 590 F.3d 1326, 1337 (Fed. Cir. 2010) ("We remind the district court and the [USPTO] Board that they must follow judicial precedent. . . ."). Thus, to the extent the USPTO examination policies are inconsistent with a final, binding ruling, the USPTO would conform its examination policies to avoid issuing patents directed to isolated DNA or the comparison or analysis of DNA sequences. See USPTO Reply Memo, at 4.

With the holding that the patents are invalid, the Plaintiffs have received the relief sought in the Complaint and the doctrine of constitutional avoidance precludes this Court from reaching the constitutional claims against the USPTO. See Allstate Ins. Co. v. Serio, 261 F.3d 143, 149-50 (2d Cir. 2001); USPTO Br. at 4. Plaintiffs' claims for constitutional violations against the USPTO are therefore dismissed without prejudice.

VIII. CONCLUSION

For the reasons set forth above, Plaintiffs' motion for summary judgment is granted in part, Myriad's motion for summary judgment is denied, the USPTO's motion for judgment on the pleadings is granted, and the claims-in-suit are declared invalid pursuant to 35 U.S.C. § 101.

Submit judgment on notice.

It is so ordered.

New York, N.Y.
March 29, 2010

ROBERT W. SWEET
U.S.D.J.