# 國立交通大學

## 科技法律研究所

## 碩 士 論 文

# Patentability of Human Genes: The *Myriad* Case and Beyond

人體基因是否可為專利保護標的:

由 Myriad 案為起點

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中 華 民 國 一〇二 年 一月

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## 摘　　要

專利制度藉由賦予研發者或投資者排他權，以達鼓勵研發之目的。此排他權可使投資者與發明者回收研究資金成本，甚至得到額外的報酬。過去三十年來，基因相關專利急速的增加，代表基因關聯發明的重要性日益增加，但也因基因專利排他的特性而對現有的科學研究產生了不良影響。例如有些基因研究因他方的專利之阻礙，無法順利進行研究。這通常涉及支付相關專利授權費用而導致基因研究的時間延長與成本提高。再從病人的角度言，當僅有專利權人可實施該技術時，可能剝奪病人獲得第二意見(second opinion)的權利。所謂的第二意見係指為了確定先前診斷報告準確性而去尋求其他意見。這些問題與專利制度鼓勵創新的本質產生了衝突，也是近期 Myriad 案之所以受到廣泛關注的原因之一。本案的主要爭點為人體基因是否可為專利保護標的，原告主要為受到基因研究專利所帶來的負面影響的研究機構與正接受臨床治療的病人，他們透過主張人體基因係非專利適格標的而使基因專利無效。本案判決代表了美國聯邦上訴法院對基因專利的最新見解，突顯出 Myriad 案的重要性。本論文之研究重點是分析美國以往專利適格標的之重要案件，並與最新 Myriad 案比較，希望藉此了解法院判斷專利適格標的之標準，哪些是一致的，而哪些是有改變的。最後，針對此判決對研究機構、病人、發明人與投資者所造成的影響，本論文將提出可行的解決方案。

關鍵字: 專利適格標的, 基因專利, 基因序列

**Patentability of Human Genes: The *Myriad* Case and Beyond**

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# ABSTRACT

The drastic increase of patent filing and applications on genes for past thirty years has shown the increased importance gene related inventions. One primary motivation of setting up the patent system is to provide an incentive to invent by insuring the investors and prospect inventors a possible return or gain of the research cost. But this exclusivity offered by gene patents has produced some adverse consequences such as the inaccessibility to genes for research, increase cost in diagnostic cost or deprive the opportunity for second opinion for patients. These are some reasons why the issue on the patentability of human genes has attracted more concern since the instigation of the *Myriad* case. The plaintiffs of this case are mainly research groups and patients that have "negatively" affected by the gene patent and therefore, hope to invalidate the patent by challenging the gene sequence not a patentable subject matter. The uniqueness and the complexity of gene patents are related to the unidentified functions in genes or broad wordings used in claims. As a result, granting gene patents may stifle the future genetic research and development of diagnostic test such as parallel sequencing and whole genome sequencing. In addition, lack of clear standards when determining patentable subject matter is also another sophisticated issue that needs to be solved when granting gene patents. Thus, the major focus of this thesis is to analyze different standards used in the precedent cases in U.S. and compare these standards with the standards used in the *Myriad* case. Thus, hope to understand Federal Court's recent view on this issue. Furthermore, discuss the implications of these new holdings on the public, investors and prospect inventors. Lastly, with different problems arise from the granting of gene patents and propose some possible solutions to help solving the current and future situation on gene patents.

Keywords: patentable subject matter, gene patents, isolated DNA sequence

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終於要畢業了!!這條路走下來真的很辛苦，但這一切都是值得的。在這段期間中，交大科法所紮實的課程設計與各位老師細心的照顧指導，讓學生有機會不斷的學習與成長。也由於這個機會，認識了一群知心的朋友。

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## Index

# Chapter 1- Introduction

## 1.1- Motive of the Research

The framers of the U.S. Constitution created incentives for technological invention by drafting Intellectual Property Clause.[1] One of major goals of the patent law is to disclose the newest scientific discoveries information to the public and to enlighten the public as to how these discoveries can benefit society.[2] However, since the first gene patent issued to Regents of the University of California in 1982 regarding a bacteria containing plasmid that expresses a chronic somatomammotropin gene[3], the debate over the protection of human gene sequence has sparked a long debate whether human genes should be treated as a patentable subject matter. One of the major concerns is the limited access to testing and diagnosis where patients are unable to confirm or verify the accuracy of the diagnostic test with another diagnostic facility when the patentee is the sole provider of the gene test.[4] Another concern relates to the potential of impeding the future researches which contradict with the original purpose of setting patent system and that is to stimulate innovation.[5]

Since the instigation of human gene research, the outcomes of the various researches have played pivotal roles in treating and preventing genetically inherited diseases. Starting in late 1970s, scientific researchers began to view genetic material as a means of developing treatment options for a variety of human diseases.[6] As the gene researches become prevalent, there is an increase trend of seeking for patent protection. Human gene sequences are now widely used in different clinical and research areas such as gene therapy, diagnostic genetic testing, and purified protein production. With the advancement of pharmaceutical industry, the relationship

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[1] The Constitution gives Congress the power to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." U.S. Const. art. I, § 8, cl. 8.

[2] Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 151 (1989).

[3] Gene Patents and Global Competition Issues, *available at* http:// www.genengnews.com/articles/chitem.aspx?aid=1163&chid=0 (last visited April. 15, 2012).

[4] David H. Ledbetter, *Gene patenting and licensing: the role of academic researchers and advocacy groups*, 10 GENETICS IN MED. 314, 314 (2008).

[5] Kate Murashige, *Patents and Research--An Uneasy Alliance*, 77 ACAD. MED. 1329 (2002) (evaluating the claim that patents such as gene patents inhibit scientific progress).

[6] MARTIN J. ADELMAN, ET AL., CASES AND MATERIALS ON PATENT LAW 59 (3d ed. 2009).

between drugs and gene product has become closer compared to a few decades ago.[7] For example, the completion of the Human Genome Project in 2003, identifying nearly 25,000 genes and 3 billion base pairs in the human body that setup a complete human gene database.[8] One of the aims of this technology is to transfer the information to private sectors, thereby facilitating diagnoses of disease and pharmaceutical development.[9] This caused a drastic increase in the number of patent applications for human genes over past few decades.[10] The number of applications increased more than double from approximately 16,000 applications in 1990 to 33,000 applications in 2000.[11] Today, close to two thirds of new drugs that reach the market have been influenced by genetic research,[12] and genetic material has been linked to more than 850 human diseases.[13] The average life expectancy of U.S. citizens has elongated and quality of life have greatly enhanced over the past century, and this largely due to the improvement of pharmaceutical and genetic innovations.[14] Nearly twenty percent of human genes are patented under United States law[15] and a

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[7] GREGORY J. HIGBY, FROM COMPOUNDING TO CARING: AN ABRIDGED HISTORY OF AMERICAN PHARMACY IN PHARMACEUTICAL CARE 19, 36-37 (Knowlton H. Calvin & Richard P. Penna eds., 2d ed. 2003).

[8] Battelle Technology Partnership Practice, *Economic Impact of the Human Genome Project* (2011), http://battelle.org/docs/default-document-library/economic_impact_of_the_human_genome_project.pdf?sfvrsn=2.

[9] *Id.*

[10] Richard Willing, *Gene Patent Gets Tougher*, USA TODAY, Nov. 15, 2000, at 14A.

[11] *Id.*

[12] Andrew Pollack, *The Genome at 10: Awaiting the Genome Payoff*, N.Y. TIMES, June 15, 2010, at B1, available at http://www.nytimes.com/2010/06/15/business/15genome.html (indicating that the Research and Development President at Bristol-Myers Squibb and the Research Executive Vice President at Roche have both proclaimed that two-thirds of newly developed drugs have been influenced by genetic research).

[13] Nicholas Wade, *A Decade Later, Gene Map Yields Few New Cure*s, N.Y. TIMES, June 13, 2010, at A1, available at http://www.nytimes.com/2010/06/13/health/research/13genome.html?pagewanted=1&ref=business.

[14] LAURA B. SHRESTHA, CONG. RESEARCH SERV., RL 32792, LIFE EXPECTANCY IN THE UNITED STATES 2-5 (2006) *available at* http://aging.senate.gov/crs/aging1.pdf (showing that the average American life expectancy has increased by nearly thirty years in the past century and citing medical advances as a reason for these decreased mortality rates); see also Kaiser Public Opinion Spotlight: Views on Prescription Drugs and the Pharmaceutical Industry 1, THE HENRY J. KAISER FAMILY FOUND. (Apr. 2008), http://www.kff.org/spotlight/rxdrugs/upload/Rx_Drugs.pdf (indicating that most American adults take prescription drugs and that a vast majority of Americans believe that prescription drugs improve quality of life).

[15] Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCI. 239, 239 (2005).

large portion of those patents related to human health especially cancer related.[16] With the increase importance in pharmaceutical development, the recent landmark case on patentability of cancer detecting gene sequence, *Association for Molecular Pathology, et al. v. United State Patent and Trademark Office, et al.* (the *Myriad* case)[17], has bought greater attention from the public and biotechnology industry on the issue of patentability of human gene sequence.

The patentable subject matter is set forth in 35 U.S.C §101. As the law stated "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 therefor, subject to the conditions and requirements of this title."[18] Attached with this rule are three major exceptions: natural phenomenon, law of nature, and abstract ideas. Those exceptions are excluded from patentable subject matter and all needed to be examined before the Court goes on to reach a conclusion as to the issue of patentable subject matter. Despite numerous preceding court decisions on this issue, prospective inventors are still left with uncertainty the standards used in determining the patentable subject matter. The recent case *Association for Molecular Pathology, et al. v. United State Patent and Trademark Office, et al*., may help to determine the most recent view of the U.S. Courts.

In this law suit, numerous non-profit organizations, research organizations and patients sued defendant Myriad and United States Patent and Trade Office (USPTO) based on the invalidity of breast cancer detecting gene patents, BRCA1 and BRCA2. The defendants' patents, which encompass composition of matter claims and process claims, were invalidated by the United States District Court, S.D. New York. However, when the case is appealed to the U.S. Court of Appeals for the Federal Circuit, district court's judgment was partly reversed because the Federal Circuit still holds the same view as expressed in the long practice of USPTO and another leading case, *Diamond v. Chakrabarty*, which supports a broad protection of bio-organisms thus "anything

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[16] *Id.* at 240.

[17] Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010); Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329 (Fed. Cir. 2011); Ass'n for Molecular Pathology v. USPTO, 132 S.Ct. 1794 (2012); Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303 (Fed. Cir. 2012).

[18] 35 U.S.C § 101 (2006).

under the sun that is made by man" is patentable.[19] The case was appealed to the U.S. Supreme Court and certiorari was granted. The case was then vacated and remanded by the Supreme Court to the Federal Court and was given an instruction to reconsider in light of *Mayo Collaborative Services v. Prometheus, Inc*. case.[20] However, in the recent verdict on remand dated Aug 16, 2012[21], the Federal Circuit still reaffirmed their previous decisions.[22] As mentioned above, this judgment by the Federal Circuit may have tremendous impact for the probability that it could bring clarity to the patentability issue regarding human gene sequences. Therefore, this case should be closely analyzed.

## 1.3 - Research scope, Method, and Structure of the Thesis

### 1.2.1 Purpose and Scope of the Research

The foundation for the U.S. patent system is based on the Article I, Section 8, Clause 8 of the U.S. Constitution which allowed the Congress to promote the progress of the science and useful arts.[23] But, the reality is showing signs that patents are not only assisting but rather partly impeding the progress of science. Since the massive patenting of ESTs (Expressed Sequence Tags) without knowing the actual function of these genes, the issue of patenting genes has become a greater issue because some scientists have argued the difficulty of developing the multiplex gene diagnostic test as it may require hundreds of genes. As more people are reliant on the biotechnology development, this issue must be resolved in order to promote greater progress of science. Via the analysis of the most recent case, *Association for Molecular Pathology, et al. v. United State Patent and Trademark Office*, on patentability of gene sequence, in hoping to determine the patentability of human gene sequence and the standards used to determine the patentable subject matter. Also, examining from a broader view, how will these recent standards set by the Federal Court may affect the future research, patient access and incentive for investment? At last, some possible solutions in

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[19] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1358 (Fed. Cir. 2011).
[20] Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 1295 (2012).
[21] Ass'n for Molecular Pathology v. USPTO, 132 S.Ct. 1794, 1794 (2012).
[22] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 39 (Fed. Cir. 2012).
[23] U.S. Const. art. I, §8 , cl. 8.

solving the future problems that can be caused by the numberless of previous granted patents.

### 1.2.2 Research Method and Structure of the Thesis

The *Myriad*[24] case has brought the attention the issue of patentability of human gene sequence. In patent law, patentable subject matter is one vital requirement for receiving a patent protection. Thus, one of the main goals of this thesis is to evaluate the standards used in precedents in determining a patentable subject matter. Standards will be categorized and analyzed via precedent cases that relate to the topic of patentable subject matter. Confirmed and disputable standards will all be discussed. These standards will be evaluated again in the new *Myriad*[25] case and compared if there are any changes to these standards.

The first chapter will introduce the motive, purpose of the research, and the research method. Chapter two includes the fundamental background knowledge on human gene sequences. A brief introduction on patent and related terms is also introduced. Chapter three focuses on the U.S judicial decision on the subject matter requirement of gene patents and why this is still an issue today. Different cases related to patentable subject matter are described and further divided into two major categories: 1) natural product in general and 2) gene in specific. Chapter four provides a detailed follow up on the *Association for Molecular Pathology v. U.S. Patent and Trade Office*[26] case. Chapter five is the issue assessment of the case and the impact that the holdings might have on people. Chapter six presents some possible solutions to the problem of gene patents and the conclusion in Chapter seven.

## Chapter 2 - Background to Gene Patent

2.1 - Fundamental Knowledge on DNA and Genome Sequencing

### 2.1.1 DNA and It's Roles

The total genetic information content of each cell is known as the genome. It

[24] Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010)
[25] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303 (Fed. Cir. 2012).
[26] *Id.*

exists within the long, coiled macromolecules of DNA.[27] DNA molecule resembles a ladder with rings and twisted into a spiral.[28] One of the major functions of the DNA is that it is a major molecular repository for genetic information.[29] The informational message is expressed or processed in two different ways: 1) exact duplication of the DNA that transfers the genetic material to daughter cells during the cell division and 2) expression of the stored information to produce RNA that are used to manufacture proteins that act as the molecular tools that carry out the cell activities.[30] For example, the proteins in the human body participate in thousands of chemical reactions that occur in one cell[31] and also act as the fundamental building blocks of cellular components.

Nucleic acids are thread like polymers which are made up of linear array of monomers call nucleotides.[32] The nucleic acid can range from 80 nucleotides to over 100 million nucleotide pairs in a single eukaryotic chromosome.[33] The unit size of a nucleic acid is the base pair (for double-stranded species) or base (for single-stranded species). Each monomer is made up of three parts: organic base containing nitrogen, a carbohydrate and a phosphate.[34] The four different kinds of organic bases include adenine (A), cytosine (C), guanine (G), or thymine (T).[35] The organic base on one side of the ladder bonds to a corresponding organic base on the opposing side called complementary base pairing.[36] Therefore, adenine (A) pair with thymine (T) and cytosine (C) pair with guanine (G) via a chemical bonding called hydrogen bond.[37] The sequence of nucleotides in a DNA strand may vary in various ways and this is what makes one organism genetic code unique. Each segment of nucleotide sequence

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[27] RODNEY BOYER, CONCEPTS IN BIOCHEMISTRY 23-33, 316-46 (3d ed. 2006).

[28] ROBERT P. WAGNER, UNDERSTANDING INHERITANCE: AN INTRODUCTION TO CLASSICAL AND MOLECULAR GENETICS, IN THE HUMAN GENOME PROJECT: DECIPHERING THE BLUEPRINT OF HEREDITY 40-41 (Necia Grant Cooper ed., 1994) [hereinafter THE HUMAN GENOME PROJECT]; JAMES D. WATSON ET AL., MOLECULAR BIOLOGY OF THE GENE 73-75 (4th ed. 1987) [hereinafter MOLECULAR BIOLOGY OF THE GENE].

[29] BOYER, *supra* note 27, at 23.

[30] *Id.*

[31] *Id.* at 23-24.

[32] MICHAEL BLACKBURN ET AL., NUCLEIC ACIDS IN CHEMISTRY AND BIOLOGY 14-15 (3d ed. 2006).

[33] *Id.*

[34] *Id.*

[35] THE HUMAN GENOME PROJECT, *supra* note 28, at 40-41.

[36] *Id.*

[37] *Id.*

is called a "gene." The gene is "expressed" when the encoded information is translated into a functional product, protein.[38]

### 2.1.2 Protein Synthesis

The gene express through a process known as "protein synthesis." During the first phase of the synthesis called "transcription," a gene serves as a template for the synthesis of a single-stranded ribonucleic acid (RNA) called a "messenger RNA" (mRNA).[39] The genes of humans contained both the protein coding sequence (called "exons") and non-coding sequence (called "introns")[40] Second phase of the protein synthesis is called "translation" where the mRNA acts as a template for the production of protein.[41] When the protein is synthesized, it can further be processed to produce necessary hormones to catalyze the chemical reactions in the body.

### 2.1.3 Duplication of DNA

Before the initial of proteins synthesis, the duplication of DNA must first take place. It is a self-directed process and the process of DNA copying is called replication.[42] The process begins with unwinding of a short segment of the two complementary strands. Each strand is then used as a template for production of a new complementary partner strand.[43] When DNA is replicated, the new copy of the DNA for the daughter cell must be identical to the parent DNA.[44] The complex replication process is not always error free; mistakes such mutations, although very rare, still occur.[45] The changes of the base sequence of DNA are called mutations and some are related to the harmful effects in human health, however, some silent mutations do not affect the function of the protein products. As the result, if the errors

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[38] *Id.*

[39] *Id.* at 45; MOLECULAR BIOLOGY OF THE GENE, *supra* note 28, at 73-75 (Transcription begins when an enzyme, an RNA polymerase, binds to a site on the gene called the "promoter." The RNA polymerase unwinds a portion of the double-helical gene, separating the gene into two strands. The RNA polymerase moves along the template strand and transcribes that strand into a single-stranded mRNA molecule.).

[40] THE HUMAN GENOME PROJECT, *supra* note 28, at 45, 64.

[41] *Id.*, at 45.

[42] BOYER, *supra* note 27, at 23-33.

[43] *Id.*

[44] *Id.* at 316.

[45] *Id.*

are allowed to be transcribed into RNA and translated, protein products are altered and therefore change the biochemical properties in the body which some developed into cancer.[46] The replication errors can be categorized into three main types: (1) substitution of one base pair for another (point mutation), (2) insertion of one or more extra base pairs, and (3) deletion of one or more base pairs.[47] Among the three types of replication errors, substitution is the most common type of spontaneous mutagenesis.[48] The gene mutagenesis is often difficult to detect without the advanced studies of genes and proper diagnostic equipment. Thus, this shows the importance of studying defective genes.

### 2.1.4 Study of Defective Genes

Numerous companies engaged in research to identify genes that associate with specific diseases like haemophilia or cystic fibrosis.[49] These diseases are caused by defect in a single gene.[50] However, there are more diseases that involve a number of different genes and result from interaction with the environment; for example, Alzheimer's disease is associated with specific genes in the sense that people carry variant of those genes have more changes of developing that disease.[51] Finding disease related genes often result from both biotechnology and genetics that involve the studies of large families with a high prevalence of the disease.[52] For example, the Mormon Church, for the religious reason, has accumulated the world's most extensive collection of genealogical data. The access to these data helped Myriad Genetics of Salt Lake City to identify the BRCA genes and their functions which associate with development of breast and ovary cancer.[53]

### 2.1.5 Cancer Genes

Mutagenesis in a gene can result with a cancer causing gene. Two general classes

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[46] *Id.*
[47] *Id.* at 330.
[48] *Id.*
[49] PHILIP W. GRUBB & PETER R. THOMSEN, PATENTS FOR CHEMICALS, PHARMACEUTICALS, AND BIOTECHNOLOGY: FUNDAMENTALS OF GLOBAL LAW, PRACTICE, AND STRATEGY 301-04 (5th ed. 2010).
[50] *Id.*
[51] *Id.*
[52] *Id.*
[53] *Id.*

of cancer genes have been identified.[54] The first class of genes that involve with the control of cell proliferation and tumor growth such as growth factors, cyclin-dependent kinase (Cdk) regulators such as cyclins, Cdk inhibitors (CKIs) and the retinoblastoma protein, apoptotic factors, and angiogenesis factors.[55] When these genes are mutated or overproduced, they will promote the abnormal accumulation of cells.[56] The second class included genes that control the stability of the genome and prevent the mutations in the first class of genes.[57] These genes are called anti-mutators genes that include DNA repair proteins, cell cycle checkpoint regulators, and genes that maintain the fidelity of chromosome segregation.[58] Two of the second class genes identified are the breast cancer susceptibility genes 1 and 2 (hereinafter *BRCA1* and *BRCA2*) which will be discussed in more details later in this thesis.[59] The second class genes expressed proteins that can perform all functions during DNA metabolism and DNA repair.[60] Conversely, there are some evidences that these proteins also participate in cell cycle checkpoint as they may stop the cell cycle progression in the presence of damaged DNA.[61]

### 2.1.6 Importance of BRCA1/2 Gene

Mutations in the BRCA1/2 genes are associated with increase risk in breast and ovarian cancer.[62] Woman with BRCA1 and BRCA2 mutations may have up to 85% cumulative risk of breast cancer, and as well as up to 50% cumulative risk of ovarian cancer.[63] 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.[64] The women with inherited

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[54] Kenneth W. Kinzler & Bert Vogelstein, *Gatekeepers and Caretakers*, 386 NATURE 761, 763 (1997).
[55] Yi Wang et al., *BASC, a Super Complex of BRCA1-Associated Proteins Involved in the Recognition and Repair of Aberrant DNA Structures*, 14 GENES & DEV. 927 (2000).
[56] *Id.*
[57] *Id.*
[58] *Id.*
[59] P.A. Futreal et al., *BRCA1 Mutations in Primary Breast and Ovarian Carcinomas*, 266 SCIENCE120-22 (1994).
[60] THE HUMAN GENOME PROJECT, *supra* note 28, at 45.
[61] *Id.*
[62] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1339 (Fed. Cir. 2011).
[63] *Id.*
[64] *Id.*

BRCA1 mutations have a 40-52% cumulative risk of ovarian cancer by the time they reach 70 years old.[65] For women inherited BRCA2 mutations, the risk is approximately 15-25%.[66] Data shows male carriers with similar mutations have increased risk for breast and prostate cancer as well.[67] All these information can help to provide the public with possible prevention for diseases such as lung cancer and ovarian cancer.

### 2.1.7 DNA Sequencing

DNA sequencing is the technique that allows the physician or scientist to uncover the information regarding the nucleotides within a DNA molecule by understanding the ordering of the nucleotide sequence. The ordering or the nucleotide can be used to determine existence of mutations that are associated with particular diseases. Genes are mostly discovered by two different methods: genomic DNA sequencing and cDNA sequencing.[68]

### 2.1.8 cDNA Sequencing

A cDNA is a sequence synthesized from an expressed gene or messenger RNA (mRNA) via a process called reverse transcription where the mRNA is transcribed[69] and this will allow the genes to be identified more efficiently because it contain only the protein coding regions (exons) and therefore it is shorter in length and less time consuming. In contrast, another type of sequencing, the genomic sequencing, deals with both non-coding and coding regions, therefore, maybe involve longer steps. The cDNAs are synthesized in vitro from mRNA. All the mRNAs are collected from various types of tissues of interest.[70] The mRNA is used as template and through the action of an enzyme called reverse transcriptase, and cDNA is produced after the reverse transcription take place.[71] Hence, one huge difference between genomic

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[65] *Id.*
[66] *Id.*
[67] *Id.*
[68] JEFFERY P. TOMKINS ET AL., DNA SEQUENCING FOR GENOME ANALYSIS, IN ANALYTICAL TECHNIQUES IN DNA SEQUENCING 158-73 (Brian K. Nunnally ed., 2005).
[69] *Id.*
[70] THE HUMAN GENOME PROJECT, *supra* note 28, at 138; Bernadine Healy, *On Gene Patenting*, 327 NEW ENG. J. MED. 664, 664 (1992).
[71] *Id.*

sequencing and cDNA sequencing is that cDNA sequencing only expresses gene fragments, exons, and not the whole gene.[72]

### 2.1.9 Whole-Genome Sequencing

Whole genome sequencing (WGS) is also known as full genome sequencing (FGS). This is the process where the entire genome is sequenced at one time by first obtaining the organism's chromosomal DNA. This is done with the aid of shotgun sequencing. This is an essential process because it allows the sub-cloning of the DNA sequencing target called library construction where it will be used afterward during comparison between each read or measurement and the library.[73] In whole genome sequencing, shotgun sequencing,[74] long strand of DNA is broken up randomly into smaller fragments by the specialized instruments or the sonication instrument,[75] which are sequenced by using the chain termination method. When multiple overlapping reads for the target DNA are detected by performing several rounds of this fragmentation and sequencing, with the help of the computer program, the full sequence can be obtained. The computer program uses the overlapping ends of different sequencing results and assembles them into a continuous sequence. The number of clones necessary to reconstruct the original target sequence depends on three factors; (1) the average length of sequence obtained from a single shotgun clone, (2) the length of the target sequence, and (3) the desired accuracy of the completed sequence.[76]

## 2.2 – Different Categories of Gene Patents

### 2.2.1 Therapeutic Protein

One of the uses for the gene sequence is to provide a production of high purity

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[72] Craig D. Rose, *Race Is on to Stake Claims to Our DNA: San Diego's Sequana Among Pioneer Firms in Fertile New Field*, SAN DIEGO UNION-TRIBUNE, Sept. 11, 1994, at A-1, A-4; Healy, *supra* note 70, at 664.

[73] Tomkins et al., *supra* note 68, at 163.

[74] R. Staden, *A Strategy of DNA Sequencing Employing Computer Programs*, 6 NUCLEIC ACIDS RESEARCH 2601 (1979).

[75] Tomkins et al., *supra* note 60, at 163-64.

[76] *Id.*

proteins via the process of transcription and translation.[77] The purified and biologically functional proteins permitted directed therapy for diseases where other therapy is not allowed.[78] Companies like Amgen and Genentech were the first to use the cloning and expression recombinant technologies to produce the human proteins that are used as drugs.[79] The products were recombinant version of human growth hormone (hGH), insulin, tissue plasminogen activator (tPA), and erythropoietin.[80] These hormones all play crucial roles in maintaining a healthy human body. For example, hGH is important in human growth because it facilitates muscle and skeletal development and insulin can regulate the glucose level in the blood.

### 2.1.10 Gene Therapy

Human gene sequence is associated to gene therapy as they provide methods which involve genes to treat diseases. As mentioned above, the abnormal protein produced by the defective gene may cause undesirable effect in the human body. Therefore, one example of gene therapy called "gene replacement" allows the change of the defective gene with proper functional gene,[81] thus prevent production of abnormal proteins. This can be achieved by modifying the gametes before ova or sperm cells are formed, thus, selecting the only desirable beneficial genes.[82] Another type of gene therapy focus on the non-reproductive cells called somatic cell gene therapy.[83] There are two main types of somatic gene therapy; *ex vivo* and *in vivo*.[84] In *ex vivo* gene therapy, cells are removed from the body, genetically modified and put back into body through the cell therapy process.[85] The first reported human trial of *ex vivo* gene therapy was carried out on a child suffering from rare form of immunodeficiency caused by the lack of a specific protein.[86] During the process, the lymphocytes from the child's blood were isolated and removed from the body. In the

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[77] HARVEY LODISH ET AL., MOLECULAR CELL BIOLOGY 102 (3d ed. 1995).
[78] *Id.* at 256.
[79] STUART O. SCHWEITZER, PHARMACEUTICAL ECONOMICS AND POLICY 57-59 (2d ed. 2007).
[80] *Id.*
[81] GRUBB & THOMSEN, *supra* note 49, at 296.
[82] *Id.*
[83] *Id.*
[84] *Id.*
[85] *Id.*
[86] *Id.*

*in vitro* process that takes place in test tubes, the vector containing the normal gene that aid the production of the specific protein is created by human intervention.[87] Then, the vector is inserted back into the patient's body to allow the production of the specific proteins.[88] The second type of gene therapy called *in vivo* gene therapy where the genes are modified within the human body without removing them from the body.[89]

The first commercial gene therapy product is called Gendicine and the main function of this product is to deliver the P53 tumor suppressor gene that is used to treat squamous cell carcinoma of the head and neck.[90]

### 2.1.11 Diagnostic testing

Diagnostic testing involves the testing of a patient's DNA sample for the presence of genetic mutation or variation correlated with some clinically significant phenotype, such as genetic disease, a propensity for cancer, or inability to tolerate a particular drug.[91] The conventional testing method used to identify a genetic variation in a DNA sample generally involve the making and using of synthetic DNA sequences corresponding to the gene of the interest, for example, the amplification and sequencing of the patient's gene or as hybridization probes.[92] The current genetic diagnostic testing methods involve making and using a polynucleotide corresponding in sequence to be fragment of interest.[93] Many genetic testing methodologies include a step in which the patient's DNA is extracted and used as a template for the production of multiple copies of the target sequence, for example, by means of PCR amplification.[94] Some testing protocols involve the direct sequencing of the patient's gene, a process that generally requires the production of copies of fragments of the

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87 *Id.*
88 *Id.*
89 *Id.*
90 張珊文等，「頭頸鱗癌基因治療結合放射治療的臨床研究」，中華腫瘤雜誌，第 29 卷第 7 期，頁 426-428（2007）。
91 Christopher M. Holman, *Learning from Litigation: What Can Lawsuits Teach Us About the Role of Human Gene Patents in Research and Innovation*, 18 KAN. J.L. & PUB. POL'Y 215, 238 (2009).
92 MOLECULAR DIAGNOSTICS: FOR THE CLINICAL LABORATORIAN 314 (William B. Coleman & Gregory J. Tsongalis eds., 2d ed. 2006).
93 *Id.* at 317.
94 *Id.*

gene sequence.[95] Other testing protocols involve the use of poly nucleotide probes that specially hybridize to know mutations of clinical relevance.[96]

## 2.3 - What Is a Patentable Invention?

U.S. Congress was given power by the constitution in Article 1, Section 8[97] to grants patents that confer a twenty year exclusive right to prevent others from making, using, offering for sale, selling or importing the patented invention in the United States. The congress has set forth U.S. patent law in the Patent Act of 1952. United States Patent and Trademark Office (USPTO) following the Patent Act to grant a patent, the fundamental principle is that the invention must fulfill the requirements of patentable subject matter,[98] useful,[99] novel,[100] non-obvious,[101] and adequately enabled and disclosed before patent can be issued.[102] Patents come in three types: utility, design and plant.[103]

35 U.S.C. §101 set forth the inventions that are patentable or the subject matter that qualifies the grant of a patent. The statue stated that "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."[104] Thus, the four statutory categories of patentable inventions are: (1) process (2) machine (3) manufacture and (4) composition of matter. All four previous categories belong to the utility patent and vary in scope protection. The focus of this thesis lies on issues of the *Myriad* case, hence, only the composition of matter patent and process patent will be further discussed. The followings are the general definitions to the four categories of utility patent.

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[95] *Id.*
[96] *Id.* at 316.
[97] U.S. Const. art. I, §8 , cl. 8.
[98] 35 U.S.C. § 101 (2006).
[99] *Id.*
[100] 35 U.S.C. § 102 (2006).
[101] 35 U.S.C. § 103 (2006).
[102] 35 U.S.C. § 112 (2006).
[103] USPTO, A GUIDE TO FILING A UTILITY PATENT APPLICATION (2008), http://www.integrityip.com/Patent_Library/USPTO/PatentFilingGuide.pdf
[104] 35 U.S.C. § 101 (2006).

### 2.3.1 Process

The words "method" and "process" are used interchangeably, but "process" is more frequently used in cases that involve chemicals, whereas "method" is more commonly used in cases that relates to mechanical and electrical products.[105] Process claim compare to product claim, can only protect the process of creation and not the end result. This means other inventors are still free to use a different process that creates the same result. According to *Gottschalk v. Benson* case, the judge defined method as process, or series of steps or acts, for performing a function or accomplishing a result[106] and according to *Muniauction v. Thomson Corp* case, a method patent claim is only infringed when a single person or entity practices all claimed steps.[107]

### 2.3.2 Machine

A machine is synonymous with an apparatus, and generally has numerous moving parts such as an internal combustion engine.[108]

### 2.3.3 Manufacture

Manufacture is usually claimed when the invention does not belong to the other three statutory categories.[109] In *Chakrabarty*, the Supreme Court did explain that main task in that case is to determine if a living organism fell within the statutory categories of "manufacture" or "compositions of matter." The Court emphasized the term "manufacture" in 35 U.S.C §101 in accordance with its dictionary definition which means 'the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery.'"[110]

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[105] ROBERT C. FABER, FABER ON MECHANICS OF PATENT CLAIM DRAFTING (2011).

[106] Gottschalk v. Benson, 409 U.S. 63, 70 (1972) ("A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing.").

[107] Muniauction, Inc. v. Thomson Corp., 532 F.3d 1318 (Fed. Cir. 2008).

[108] JANICE M. MUELLER., INTRODUCTION TO PATENT LAW 213 (2d ed. 2006).

[109] *Id.*

[110] Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980).

### 2.3.4 Composition of Matter

Composition of matter claim is one type of utility patent. Prior to the grant of utility patent, patentable subject matter must first qualify and the scope of patent is then determined. When referring to a gene patent scope, it covers the physical compositions include the gene itself. As the result, composition of matter claims may thwart the public from using genes that fall within the scope of claims. Hence, composition of matter claims can prevent others from extracting or isolating these genes from the genome by any means. The court in *Chakrabarty* case gave a general definition for the composition of matter claim: "all compositions of two or more substances and ….all composite articles, whether they be the results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids."[111] The term "composition of matter" is primarily used in pharmaceutical patents. It can be a chemical compositions and mixtures of substances such as metallic alloys.[112] Composition claims are generally very specific. If a composition of matter is claimed, it is the physical structure of the composition that must be novel, not merely its properties.[113]

## 2.4- Gene Patent and It's Different Perspectives

### 2.4.1 Definition of Gene Patent

The U.S. Patent and Trademark Office (USPTO) grants patents on human gene sequences, that grants patent holders with the exclusive rights to those genetic sequences, their usage, and their chemical composition. Therefore anyone who makes or uses a patented gene is committing an infringement without permission of the patent holder, no matter whether it is for commercial or noncommercial purposes.

The definition of a gene patent in this thesis will include the different types of patent claims directed to synthetic genetic constructs that includes the genetic sequence and methods of using those genetic sequences. Synthetic genetic constructs refers to the genetic information in a physical form, including DNA molecules and

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[111] *Id.*
[112] *Id.*
[113] Holman, *supra* note 91, at 225.

proteins themselves. Methods of using genes include using the particular genes to treat diseases, or as tools for disease detection or diagnostic.

### 2.4.2 Incentives to Invest

The important function of the patent system is to provide the incentive to invest in the development and commercialization of biotechnology and gene patent derived inventions because the right of exclusion assures the inventor that within the twenty year patent term, his/her invention will be well protected.[114] Establishing fundamental understanding of scientific process and fostering a viable biotechnology industry require large amount of investments because it demands accumulation of years of research from academic, government and private sectors. The complexity of biological products may present risk not known until late in the clinical investigations or even worse after the product has been marketed and used by a larger population.[115] This is one unique characteristic about biotechnology industry. Also, each gene may participate in different roles in the body. Thus, there is a possibility a gene maybe first patented but some unknown functions are not discovered when gene was first patented.

Nonetheless, there is an underlying theory that "the patent system is not so much needed to stimulate inventive activity; rather, it facilitates investment into costly and risky development processes that are necessary to transform a 'mere' invention into a marketable product."[116] One example to oppose this theory is the defendant of the *Myriad* case, Myriad Genetics Company, was largely financed by private venture capital totaling at least 22 million dollars.[117] Research funded by private venture capital may rely more on patent than the government or public funded research. In 2007, over $7 million in venture capital was invested in biotechnology startups.[118] The solution to secure venture capital for the bio-entrepreneurs was obtaining the

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[114] Wolrad Prinx zu Waldeck und Pyrmont, *Research Tool Patents After Integra v. Merck – Have They Researched a Safe Harbor?* 14 MICH. TELECOMM. & TECH. L. REV. 367, 272 (2008).

[115] LI WESTERLUND, BIOTECH PATENTS, EQUIVALENCE AND EXCLUSIONS UNDER EUROPEAN AND U.S. PATENT LAW 10 (2002).

[116] *Id.* at 372.

[117] Larry A. Roberts, *Myriad: How Did Public Policy Weigh In?*, INTELL. PROP. STRATEGIST, May 2010, at 1, 5.

[118] Stacy Lawerence, *2007- A Banner Year for Biotech*, 26 NATURE BIOTECHNOLOGY 150, 150 (2008).

patent protection over their biological product.[119] Without patents, the ability to attract the necessary investment would be greatly diminished.[120] The private capital investments are often required for small biotechnology companies to survive because these enterprises have very limited or no revenue to conduct the research.[121] The continuation of their researches depends on venture capital and public market investors.[122] Without the existence of patents, important researches may be delayed or never would have existed. This, in the long run, lead to stagnation in product development because small biotechnology companies play an important role in bridging the gap between basic scientific discoveries and the development of marketable products based on those discoveries.[123] As Rebecca Eisenberg stated in her article, patents are purposed to allow "inventors to use their monopoly positions to exact a price that more closely approaches the value that users receive from inventions."[124]

Also, without the protection of patents, biotechnology companies would likely to rely solely on trade secrets.[125] This would severely reduce the innovative advancement for biotechnologies. People who are against the patenting of gene sequence may have failed to appreciate the emerging biotechnologies. Being able to manipulate gene expression in fact has some therapeutic benefits. For example, RNAi, known as RNA interference, the function of this mechanism used in the natural organisms is to silence the gene activity.[126] This discovery allowed the scientists to develop an easy and specific method to manipulate gene expression.[127] RNAi has

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[119] Chrisopher J. Betti, *Diagnostic Genetic Technologies Left Stranded on First Base: A Need to Unwind the Protection Afforded Gene Patent*s, DUPAGE COUNTY BAR ASS'N BRIEF, 22, 23 (2005).
[120] *Id.*
[121] Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Courts and Intellectual Propery of the H. Comm. on the Judiciary, 106th Cong. 74 (2000) (statement of Dennis J. Henner, Ph.D., Senior Vice President, Research, Genetech, Inc.), *available at* http://commdocs.house.gov/committees/judiciary/hju66043.000/ju66043_0f.htm.
[122] *Id.*
[123] Iain M. Cockburn, *The Changing Structure of the Pharmaceutical Industry*, 23 HEALTH AFF. 10, 15 (2004).
[124] Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1046-48 (1989).
[125] Michael John, Gulliford, *Much Ado About Gene Patents: The Role of Foreseeability*, 34 SETON HALL L. REV. 711, 730 (2004).
[126] Scott E. Martin & Natasha J. Caplen, *Applications of RNA Interference in Mammalian Systems*, 8 ANN. REV. GENOMICS HUM. GENETICS 81, 82 (2007).
[127] *Id.*

therapeutic role in treating malignant, infectious and autoimmune disease.[128]

In January 2008, scientists at the J. Craig Venter Institute published a report describing the first synthetically created bacterial genome.[129] This synthetic biology has the potential to create microorganism capable of producing inexpensive medical therapies such as malarial vaccines or environmentally friendly industrial materials. Also, more research is still under way to produce synthetic organisms for use as highly efficient bio-fuels that reduce the environmental cost to produce fuels.

Even though both RNAi and synthetic biology are very diverse technologies, but they share the commonality and that is the both technology require protection of gene patents. Gene patents in these two technologies played an essential role to ensure the useful application will result. Biologics also known as biopharmaceutical drugs currently make up approximately 40% of all preclinical candidates.[130] The biologics market is expanding at a faster rate than the conventional drug market.[131] The high cost in research and development make the patents absolutely indispensable in providing the necessary incentive to invest.[132]

Celera, a manufacturer of diagnostic products emphasized "even though the Draft Report suggests that scientists who search for gene-disease associations may not be motivated by the prospect of receiving a patent, they cannot conduct this type of research without considerable capital and resources.[133] Celera quoted, "in our experience, meaningful gene disease associations are confirmed only if the initial discoveries are followed by large scale replication and validation studies using multiple sample sets, the costs of which are prohibitive for many research groups. Private investors who provide funding for such research invariable look to patents that

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[128] Charles X. Li et al., *Delivery of RNA Interference*, 5 CELL CYCLE 2103 (2006).

[129] J. CRAIG VENTER INSTITUTE, FIRST SELF-REPLICATING SYNTHETIC BACTERIAL CELL (2009), http://www.jcvi.org/cms/fileadmin/site/research/projects/first-self-replicating-bact-cell/fact-sheet2.pdf.

[130] Stacy Lawrence, *Pipelines Turn to Biotech*, 25 NATURE BIOTECHNOLOGY 1342 (2007).

[131] Saurabh Aggarwal, *What's Fueling the Biotech Engine?*, 25 NATURE BIOTECHNOLOGY 1097 (2007).

[132] Christopher J. Betti, *Diagnostic Genetic Technologies Left Stranded on First Base: A Need to Unwind the Protection Afforded Gene Patents*, DUPAGE COUNTY BAR ASS'N BRIEF, April 2005, 22, at 23.

[133] Sec'y's Advisory Common. on Genetics, Health, & Soc'y, GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 23 (2010), http://oba.od.nih.gov/oba/sacghs/reports/sacghs_patents_report_2010.pdf [hereinafter SACGHS report].

result from such work as a way of protecting their investment."[134]

People who reject the patentability of gene patents may argue that even though patents are required to attract investment, but 67% of the patents issued for discoveries on genetic diagnostics are government or university funded.[135] For the scientists and researchers that belong to government or university, desire to advance understanding, hope to improve patient care and career advancement may be their primary motivations.[136] For example, International HapMap Project that identified genes that relates to age macular generation and autism where NIH National Institute of General Medical Sciences for providing funding and support for cell line transformation and storage in the NIGMS Human Genetic Cell Repository at the Coriell Institute.[137]

They may also argue genetic diagnostic are unlike pharmaceutical patents in which pharmaceutical products must require significant investment before obtaining the approval from FDA. The costs are generally considered minimal. The government and university sponsorship including international collaborations like the Human Genome Project and HapMap Project can result a decrease in research cost.[138] However, expensive clinical trials are still needed for the genetic tests. However, even more relaxed standards decrease the price of clinical trials for the genetic testing, it is estimated that is requires approximately half of the $802 million price tag, which is nearly $454 million.[139] However even these examples show that Federal Government is the most likely to be the major funder of basic research but there is no definitive data on Federal Government versus private sector investment in basic genetic research.[140]

Even though the development of genetic tests is lower compare to drugs because of several reasons mentioned above. However, this does not wipe out the possibility that patents are still required to protect the risky investment. The less overall cost of

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[134] *Id.*

[135] Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 210 (S.D.N.Y. 2010).

[136] SACGHS report, *supra* note 133, at 32.

[137] Int'l HapMap Consortium, *A Haplotype Map of the Human Genome*, 437 NATURE 1299, 1301 (2005).

[138] Andrew S. Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, NORTHWESTERN JOURNAL OF TECHNOLOGY & INTELLECTUAL PROPERTY 12 (2011).

[139] *Id.*

[140] SACGHS report, *supra* note 133, at 51.

developing genetics may still remain to be a significant amount for the small biotechnology company. Whether the issuing of gene patents provides the necessary incentive remain to be further discussed below.

### 2.4.3 Patient Access

One concern of gene patents is that they may hinder access to medical treatment or tests.[141] The gene holder controls any use of its gene. The patent holder can prevent doctors or researchers from testing a patient's blood. The gene patents have increased the genetic test cost that has diminished the patient access especially when patient's insurance does not cover the test. One possible reason is that the insurance providers directly bear the burden of increased cost when there is a lack of competition created by only having a sole provider. Also, with the possible increase in research cost, the increased cost maybe passed on to the patients and insurance providers. The limited access affects the quality and accuracy of those tests. When exclusive right granted to the patent holder, like *Myriad* case[142], this will likely to result that only one laboratory can perform the diagnostic or research test. This will cause decrease opportunity for patients searching for second opinion test and this may affect patients' access to better quality testing. The reason is that patients are unable to assess the accuracy of the previous diagnostic test by comparing the test results when the test is only offered by one sole provider. Different providers may provide different test methods of test method or improvement of it. Without competition, there is less incentive to improve the genetic test and thus, the optimal performance may not be achieved.[143] The *Myriad* case involves patenting cancer detecting human gene, BRCA genes[144], may have similar effect as well. Many of plaintiffs in that case are patients that were disturbed from access to the diagnostic test. Many patients couldn't seek for second opinion examination before pursuing mastectomy and hysterectomy. Also, the high cost resulting from the protection of patent is preventing many patients' from access to the diagnostic test because the some insurance companies are

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[141] *Id.* at 15.

[142] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1339 (Fed. Cir. 2011).

[143] Steve Nenowitz, *French Challenge to BRCA1 Patent Underlies European Discontent*, 94 J. NAT'L CANCER INST. 80, 80-81 (2002).

[144] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1339 (Fed. Cir. 2011).

unwilling to cover such a high expense. Studies from the past few years have shown between 19% and 74% of patients who could benefit from the BRCA testing were not tested.[145] Health plans helped to reduce the number of patients who use their own pocket money to pay for the BRCA test.[146] For the women whose costs of the tests were covered by their insurance or Myriad programs, only 70% of them already had the BRCA test.[147] In contrast, only 22% from patients who pay from their pocket chose to receive the diagnostic test.[148] With the protection of patent, the diagnostic test is five times more expensive in the U.S. than in France,[149] where the BRCA gene patents were ruled invalid.[150] French physicians also alleged that Myriad's tests only assess 10-20% of the potential mutations in the gene[151] and French physicians are able to find mutations that Myriad missed.[152] The study practitioners in the U.S. performing genetics tests on a daily basis collectively feel that the cost for patients have increased dramatically due to patent protection and in turn have an adverse effect on the access of patients.[153]

Athena Diagnostics has used its exclusive rights to various hearing loss genes to stop some laboratories from testing and with Alzheimer disease as well.[154] The company holds the exclusive license of the gene and it would not let anyone to perform the test. Doctors were sued across the country where they have to try to determine if their patients have the genetic form of Alzheimer.[155] Another example

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[145] Shannon Kieran et al., *The Role of Financial Factors in Acceptance of Clinical BRCA Genetic Testing*, 11 GENETIC TESTING 101, 101 (2007); Complaint at 19, 22-25, Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181 (S.D.N.Y. 2010).

[146] *Id*. at 102.

[147] *Id*.

[148] *Id*.

[149] Robert Cook-Deega et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 GENETICS MED. S15, S28 (2010).

[150] *Id*.

[151] Declan Butler and Sally Goodman, *French Researchers Take a Stand Against the Cancer Gene Patent*, 413 NATURE 95, 95 (2001).

[152] Sophie Gad et al., *Identification of a Large Rearrangement of the BRCA1 Gene Using Colour Bar Code on Combed DNA in an American Breast/Ovarian Cancer Family Previously Studied by Direct Sequencing*, 38 J. MED. GENETICS 288 (2001).

[153] Mildred K. Cho et al., *Effects of Patents and License on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS3, 5 (2003).

[154] SACGHS report, *supra* note 133, at 33.

[155] *Id.*

like Miami Children's Hospital enforced its patent on the Canavan disease gene resulting laboratories stopping testing for patients.[156] Canavan disease is a rare genetic disease that occurs frequently in Ashkenazi Jewish that can lead to a degeneration of the brain, causing the children to lose their vision, suffer with seizures and eventually require tube feeding.[157] In this case, the holder of the patent demands a higher than-usually-royalty and tried to control the number of tests permitted.[158] This ultimately affected the patients' access to genetic testing. In comparison, the countries where such gene is not patented, the doctors are able to discover previously unknown mutations by performing the genetic test.[159]

### 2.4.4 Research Access

There is a concern that "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"[160] Michigan's law Professors Michael Heller and Rebecca Eisenberg pointed out how patents can deter innovation in biomedical research: "A proliferation of intellectual property rights upstream may be stifling life saving innovations further downstream in the course of research and product development."[161] The limited monopolies granted by the gene patents and exclusive licensing have created decrease in competition all hinder patient access to gene related diagnostic.

In the case of granting method patents, for example, in one of the U.S 5,693,470 patent claims "a method of determining a predisposition to cancer comprising: testing a body sample of a human to ascertain the presence of a mutation in a gene identified as hMSH2.[162] The patent claims "testing" and this generally refer to, any testing method, including any multiplex testing that "ascertains the presence"

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156 *Id.*
157 *Id.*
158 *Id.*
159 Andrea Knox, *The Great Gene Grab: Firms Toss Researchers for a Loop,* PHILADELPHIA INQUIRER, Feb. 13, 2000, at A1.
160 Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 208 (S.D.N.Y. 2010).
161 Michael A. Heller and Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698-701 (1998).
162 *Id.*

of a mutation in hMSH2 would probably infringe this patent claim.[163] Some clinical laboratories are forced to stop the research due to the enforcement of patents. The result of a research done by Kyle Jensen and Fiona Murray showed that nearly 20% of human genes are explicitly claimed in the U.S. as intellectual properties.[164] This indicates 4,382 out of the 23,688 of genes protected by patent rights and these genes are claimed in 4,270 patents within 3,050 patent families and owned by 1,156 different assignees.[165] 63% of these patents are assigned to private firms and out of top ten gene patent assignees, nine are U.S. based.[166] The top patent assignee is Incyte Pharmaceuticals who has IP rights cover 2,000 genes, mainly used on microarrays and DNA probes which microarrays may require multiple genes. This underlies a potential problem when a segment of gene belongs to multiple patent owners.[167]

The cost could increase when research laboratory is forced to send multiple samples to different sole test providers.[168] Also, the increased cost may due to the laboratory expense on researching if the genes are patented and if so, how are they are licensed.[169] The Emory Molecular Diagnostic Laboratory suffers with licensing problem.[170] The companies that permit sublicensing of gene patents, some require upfront license fees or a fee per sample.[171] Also, there are sublicenses that restrict the laboratory use of the patents such as limiting the test performed only on in-house patients.[172] Another concern of granting gene patents lies when there is a need to acquire the license from multiple patent owners for the developing of multi-genetic tests, parallel sequencing and whole genome sequencing. By granting a patent to one of the gene sequence may inhibit further study of diagnostic test due to expensive

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163 *Id.*

164 Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, SCIENCE 310, 239-40 (2005).

165 *Id.*

166 *Id.*

167 *Id.*

168 Karen P. Mann, *Gene Patents: Perspectives from the Clinical Laboratory*, 14 MOLECULAR DIAGNOSIS & THERAPY 137, 139 (2010).

169 SACGHS report, *supra* note 133, at 41.

170 Karen P. Mann, *supra* note 168, at 138.

171 *Id.*

172 *Id.*

negotiating licenses.[173] With the increase in patent numbers, the broader protection on the genetic sequences may eventually affect the overall research by the physicians.[174]

Mildred Cho and four other researchers conducted an experiment on the effects of patents and license on the provision of clinical genetic testing services.[175] The respondents included companies, universities, and hospitals.[176] Out of 132 respondents, 65% percents of respondents indicated that their laboratories had been contacted by patent or license holder regarding patent infringement and 53% have decided not to develop or perform a test/services for clinical or research purposes because of patents.[177] These studies clearly show that the access to research is clearly influenced by the existence of gene patents.

# Chapter 3 - U.S Judicial Decisions on Patentability of Gene Patent

## 3.1 - Focus on Patentable Subject Matter

Under 35 U.S.C § 101, the invention patentable includes four independent categories of inventions or discoveries that are eligible for protection: processes, machines, manufactures, and compositions of matter[178]. Even though the four categories are clearly set forth in the statue, but there is still lacking a clear line in determining the patentable subject matter. The following is the analysis on previous U.S cases related to the patentable subject matter. The rationale from each case regarding to the same issue will be grouped together and compared. Then, the well accepted standards will first be introduced. In addition, the debatable standard and the disagreement between the decisions of each case will be further discussed in the latter analysis.

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[173] Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998).
[174] Cho, M., *Ethical and legal issues in the 21st Century: Preparing for the Millennium: Laboratory Medicine in the 21st Century.* Orlando: AACC PRESS, 47–53 (1998).
[175] *Id.* at 50.
[176] *Id.*
[177] *Id.*
[178] 35 U.S.C § 101 (2006).

### 3.1.1 Well Accepted Standard Prior to the *Myriad* Case

#### 3.1.1.1 Exceptions to Patent Act

The issue of whether laws of nature, physical phenomena and abstract ideas can be patented has been consistently ruled by the U.S. court. Even though these three exceptions are not stated in the statutory text, however, this standard is clearly set forth in another landmark case on gene patent; the *Chakrabarty* case.

Case 1 - *Funk Bros. Seed Co. v. Kalo Inoculant Co.* (1948)

In *Funk Bros. Seed Co v. Kalo Inoculant Co.* case, patentee Bond, was granted a Patent No. 2,200, 532 with product claim on May 14, 1940 and petitioner filed a counterclaim of a declaratory judgment that the entire patent should be deemed as invalid.[179] The leguminous plants, with the presence of bacteria called *Rhizobium* are capable of nitrogen fixation located on the plant roots from the air and then convert that air nitrogen into nitrogenous compounds that are beneficial to the plant.[180] Each type of bacteria infects only particular groups of plants and no species of bacteria was found that can infect all types of plants.[181] Methods of selecting the strain of bacteria and reproducing them were well known before this case and the previous manufacture inoculants only contain one species of the bacteria.[182] Therefore, if the farmers need to cross inoculate three types of crops then they need to use three separate inoculants.[183] Thus, mixed cultures were used but the result was unsatisfactory due to the mutually inhibitive effect on each bacteria.[184] The patentee of this case found the mutually non-inhibitive strains that can be used in mix cultures, therefore, capable of inoculating the plants seeds at one time.[185] The court explained that patentee did not create state of inhibition or of non-inhibition in the bacteria.[186] The qualities of their invention are work of nature and of course not patentable.[187] For patents cannot issue

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[179] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).
[180] *Id.*
[181] *Id.*
[182] *Id.*
[183] *Id.*
[184] *Id.*
[185] *Id.*
[186] *Id.*
[187] *Id.*

for the discovery of the phenomena of nature.[188] The qualities of the bacteria are "like the heat of the sun, electricity, or qualities of metals are part of the storehouse of knowledge of all men."[189] They are "manifestations of laws of nature, free to all men and reserved exclusively to none."[190] Simply the discovery of unknown phenomenon of nature cannot be granted patent.[191] Supreme Court clearly holds that the discovery of the fact that certain strains of bacteria be mixed without producing harmful effect is simply no more than discovery of some of the handiwork of nature and hence is not patentable.[192]

Case 2 - *Gottschalk v. Benson* (1972)

The application of the patent involves a method for converting the binary coded decimal numerals into pure binary numerals for use with digital computer.[193] The application was rejected by examiner and again rejected by the Board of Appeals.[194] The case was granted certiorari and the Supreme Court held the computer program, a mathematical formula without substantial practical application except in connection with digital computer, was not a patentable process.[195] The court stated that in *Mackay Radio & Tel. Co. v. Radio Corp.* case, that "while a scientific truth, or the mathematical expression of it, is not patentable invention, a novel and useful structure created with the aid of knowledge of science truth may be."[196] Also, the court clearly indicated that 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.[197]

Case 3 - *Diamond v. Chakrabarty* (1980)

Chakrabarty is a microbiologist who invented "a bacterium from the genus

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[188] Le Roy v. Tatham, 55 U.S. 156, 175 (1852).
[189] Mackay Radio & Tel. Co. v. Radio Corp. of Am., 306 U.S. 86, 94 (1939).
[190] *Id.*
[191] *Id.*
[192] *Id.*
[193] Gottschalk v. Benson, 409 U.S. 63, 67 (1972).
[194] *Id.*
[195] *Id.*
[196] Mackay Radio & Tel. Co. v. Radio Corp. of Am., 306 U.S. 86, 94 (1939).
[197] *Id.*

*Pseudomonas* containing therein at least two stable energy generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway."[198] This invention or bacterium is capable of breaking down multiple components of crude oil and therefore used commonly for the treatment of oil spills.[199] The plasmids are hereditary material that's found commonly in bacteria and once plasmid is inserted into a specific vector then this will allow the vector to perform the function of this plasmid. This discovery of this function in different bacteria allows them to degrade different types of oil component. These plasmids were inserted into a vector called *Pseudomonas* bacterium which originally doesn't have the ability to degrade oil.[200] As a result, this invention can be used as treatment to oil spills where oil is degraded. The patent claims included three types. Only one category was rejected, and that was the claims for bacteria itself. The decision was supported by two main reasons. The first reason is that micro-organisms are "product of nature" therefore un-patentable.[201] The second reason is that living things are not patentable subject matter under 35 U.S.C. §101.[202]

In 1952, when the patent laws were re-codified, the Congress intended statutory subject matter to "include anything under the sun that is made by man."[203] Nevertheless, this is not to suggest that 35 U.S.C. §101 has no limits or that it embraces every discovery.[204] The laws of nature, physical phenomena, and abstract ideas have been held not patentable.[205] Therefore, the new mineral discovered in the earth and the new plant found in the wild are both not patentable subject matter.[206] Also, the law of gravity discovered by Newton is also excluded from patentable subject matter because these discoveries are "manifestations of …nature, free to all men and reserved exclusively to none."[207] The court held that a man-made, living microorganism is a patentable manufacture or composition of matter within the

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198 Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
199 *Id.*
200 *Id.*
201 *Id.*
202 *Id.*
203 *Id.*
204 *Id.*
205 *Id.*
206 *Id.*
207 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

meaning of 35 U.S.C. §101.[208]

### 3.1.1.2 Application of a Law of Nature or Mathematical Formula May Deserve Patent Protection

Case 1 – *Mackay Radio & Tel. Co. v. Radio Corp. of Am.* (1939)

Patent in suit is a directive antenna system for use in radio communication and it consisted in taking the angle of the Abraham formula as the angle between each wire of the V antenna and its bisector.[209] This allows placement of cones of principal radio activity, each having one of the wires of the antenna as its axis, into conjunction at their periphery and along the bisector of the angle between the wires, and thus established the greatest directional radio activity.[210]

The Court declared that "while a scientific truth, or the mathematical expression of it, is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be."[211] This advance was achieved by the logical application of a known scientific law to a familiar type of antenna.[212] However, the Court held that "the attempt to broaden the invention described in the application through a purely mechanical alteration of the meaning of the empirical formula cannot be taken to enlarge the description of the invention as measured by the Abraham formula, so to include a structure to which that formula does not apply."[213]

Case 2- *Funk Bros. Seed Co. v. Kalo Co.* (1948)

The inhibition or non-inhibition qualities of the bacteria are like "heat of the sun, electricity, or the qualities of metals, are all part of the storehouse of knowledge of all men."[214] Those qualities are "manifestations of laws of nature free to all men and reserved exclusively to none."[215] "He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If

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[208] Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
[209] Mackay Radio & Tel. Co. v. Radio Corp. of Am., 306 U.S. 86, 91 (1939).
[210] *Id.*
[211] *Id.*
[212] *Id.*
[213] *Id.*
[214] *Id.* at 94.
[215] *Id.*

there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end."[216]

Case 3- *Diamond v. Diehr* (1981)

The Court held that while a claim drawn to a fundamental principle is not patentable, on the other hand, "an application of a law of nature or mathematical formula to a known structure or process may well deserve patent protection."[217] The new method for molding raw, uncured synthetic rubber into cured precision products, by using a "mathematical formula" may deserve patent protection.[218] Also, the invention must be considered as a whole rather than "dissecting the claims into old and new elements and then…ignoring the presence of the old elements in the analysis."[219]

## 3.2 Issues at Debate Prior to The *Myriad* Case

### 3.2.1 Standard for the Distinction Between Product of Nature and Human-made Invention

3.2.1.1 – Natural Product in General

Case – 1 *Hartranft v. Wiegmann* (1887)

In this case, the defendant moved for a new trial due to the court's decision that in order to render the shells subject to duty as 'manufactures of shells,' *something more* must be done than simply to remove the outer surface either by acids or mechanical means, and that, while the shells *retained their special form and character*, therefore invention could not be classified as manufactures of shells.[220]

The Court stated the question lies where whether cleaning off the outer layer of the shell by acid, and then grinding off the second layer by an emery wheel, so the brilliant inner layer can be exposed, is a manufacture of the shell.[221] The purpose of

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[216] *Id.*
[217] Diamond v. Diehr, 450 U.S. 175, 187 (1981).
[218] *Id.* at 184.
[219] *Id.* at 189.
[220] Hartranft v. Wiegmann, 121 U.S. 609, 612 (1887).
[221] *Id.*

these *manipulations* is to produce ornaments.[222] Not only the shells were sold for ornaments but also used to make buttons and handles of penknives.[223] However, there is no difference in *name and use* between the shells before the process by the emery wheel and those are not.[224] However, It is contended by the government that shells are prepared by the mechanical or chemical means stated in the record, for ultimate use, are manufactures of shells, and thus, within the meaning of the statute.[225]

The Court held shells are still shells. They had not been manufactured into a new and different article that should have a *distinctive name, character, or use* from that of a shell.[226] "The application of labor to an article, either by hand or by mechanism, does not make the article necessarily a manufactured article, within the meaning of that term as used in the tariff laws."[227] Washing and scouring wool does not make the resulting wool a manufacture of wool, and cleaning and ginning cotton does not make the resulting cotton a manufacture of cotton.[228]

Case 2 - *Parke-Davis v. Mulford Co.* (1911)

Jokichi Takamine is the patentee of two patents which one is the isolation of a purified substance, Adrenalin, from the suprarenal glands of animals.[229] The alleged infringements of the defendant consist of two products. The first product is dry powder which constitutes the active chemical principle of the suprarenal glands.[230] The second product is the sodium chloride solution of the borate.[231] The patentee claims that the both defendant's products had infringed his first patent and second patent.

The main issue in this case is whether merely an extracted product without change can be patentable. The Court held, the patent is only for a degree of purity and therefore not for a new "composition of matter."[232] But, even if the invention is

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[222] *Id.*
[223] *Id.*
[224] *Id.*
[225] *Id.*
[226] *Id.*
[227] *Id.*
[228] *Id.*
[229] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 97 (S.D.N.Y. 1911).
[230] *Id.* at 108.
[231] *Id.*
[232] *Id.* at 103.

extracted product without change, there is no rule that such products are not patentable.[233] Patentee was the first to make it available for any use by removing from gland tissue in which it was originally found and therefore it is logically to call this a purification of the principle. This invention became for every practical purpose a *new* thing "commercially and therapeutically", which is a good ground for a patent.[234]

Case 3 - *American Fruit Growers v. Brogdex Co.* (1931)

The invention is an art that prepares fresh fruit for the market especially citrus fruits and fruits that are vulnerable to the development of molds.[235] The infection of the molds or mold's spores is prevented by the complete treatment with a mold inhibiting reagent comprising the boric acid radical.[236] The attachment of boric acid compound onto the fruit can slow down or inhibit the activity of blue mold. This can assist to prolong the fruit's freshness and flavor for longer period of time.[237] In this case, the Court held that addition of borax to natural fruit does not produce from the raw material an article for use which posses a *new* or *distinctive form, quality* or *property*.[238] The addition of the boric compound only protects the natural fruit against deterioration by inhibiting development of the mold's spores. There is no change in the name, appearance or general character of the fruit.[239] The fruit remains the same beneficial use. The Court stated that there must be a transformation; a new and different article must emerge "having a distinctive name, character, or use."[240]

Case 4 - *Funk Bros. Seed Co. v. Kalo Co.* (1948)

The patentee had discovered the existed natural species of root nodule bacteria that do not exert a mutually inhibitive effect on each other.[241] The Court stated that the patentee had discovered "only some handiwork of nature" and therefore the

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233 *Id.*
234 *Id.*
235 American Fruit Growers v. Brogdex Co., 283 U.S. 1, 5 (1931).
236 *Id.* at 7.
237 *Id.* at 9.
238 *Id.* at 11.
239 *Id.* at 12.
240 *Id.*
241 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

product is not a patentable subject matter.[242] In the rationale, the Court expressed "each species of root nodule bacteria contained in the package infects the same group of leguminous plants which it always infected.[243] No species acquires a different use.[244] The combination of species produces no new bacteria, no new changes in six species of bacteria, and no enlargement of the range of their utility.[245] Each species produced the same effect it always had in their natural state.[246] Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee."[247]

Case 5 – *In re* Marden (1998)

The patent application of John Wesley Marden involves the production of vanadium that is ductile.[248] The patent claims by taking oxide of vanadium and reducing it to the form of vanadium powder.[249] Then the powder is slowly heated in a high vacuum until all the adsorbed gases such as hydrogen is removed.[250] At last, a filament is formed by cold working the fused body of vanadium.[251]

One of the central issues is whether patentee has invented a *new and useful* process for producing pure vanadium entitled to a patent. In the rationale of the Court, it declared the quality of purity or ductility is a quality of natural product, vanadium.[252] The Court also acknowledged that, the purification of the vanadium brings about its ductility nonetheless, the ductility or malleability of vanadium is one of its inherent or natural characteristics and held not patentable.[253]

3.2.1.2 – Gene Patent in Specific

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[242] *Id.* at 132.
[243] *Id.* at 130.
[244] *Id.* at 131.
[245] *Id.*
[246] *Id.*
[247] *Id.*
[248] *In re* Marden, 47 F.2d 958, 958 (C.C.P.A. 1931).
[249] *Id.*
[250] *Id.*
[251] *Id.* at 959.
[252] *Id.*
[253] *Id.* at 960.

Case 1 - *Diamond v. Chakrabarty* (1980)

The bacteria invented by patentee were genetically engineered with at least four naturally occurring DNA plasmids, each of which enabled the decomposition of different components of crude oil.[254] This ability or character does not occur in a single naturally bacterium that may efficiently break down the crude oil in oil spills.[255] The Supreme Court held that bacteria as patentable subject matter because the "claim is not to a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter – a product of human ingenuity 'having a distinctive name, character and use.'"[256]

Case 2 - *Amgen, Inc v. Chugai pharmaceutical co.* (1991)

This case was an appealed from the judgment of the United States District Court for the District of Massachusetts and the case involves issues of patent validity, infringement and inequitable conduct with two patents: U.S. Patent 4,703,008 ('008) owned by Amgen Inc, and U.S. Patent 4,677,195 ('195) owned by Genetics Institute, Inc.[257] The plaintiff, Amgen Inc (Amgen) is the owner of DNA sequences encoding Erythropoietin (EPO) and the defendant includes, Chugai Pharmaceutical Co., Ltd., and Genetics Institute who is the owner for method of purification for EPO and EPO compositions.[258] The Court finally held the plaintiff's patent was not obvious, satisfied best mode requirement and did not satisfied enablement requirement. In contrast, the defendant's patents were not adequately enabled.[259] According to the USPTO's standard in granting a patent, patentable subject matter is one of the elements required in determining a valid patent. However, other elements in qualifying the patent are considered in this case except the issue of the patentable subject matter. This may lead to an inference that patent for EPO DNA sequence and method for purification for EPO and EPO compositions qualify the patentable subject matter.

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[254] Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
[255] *Id.*
[256] *Id.*
[257] Amgen, Inc., v. Chugai Pharmaceutical co., Ltd., and Genetics Institute, Inc., 927 F.2d 1200, 1203 (Fed. Cir. 1991).
[258] *Id.*
[259] *Id.*

Within the '195 patent, one of the claims stated that "a pharmaceutical composition for treatment of anemia comprising a therapeutically effective amount….a pharmaceutically acceptable vehicle."[260] The similar standard was used in *Parke-Davis v. Mulford Co.* case in which the invention of more purified product was granted a patent on the bases that lead to commercially and therapeutically effective result. Thus, this shows a similar standard of granting a patent in distinguishing the natural product from the human made invention.

Also, in Patent 4,703,008, the claim 6 claimed that "a prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 5."[261] This claim may indicate the transformation requirement to distinguishing the natural product and human made invention. In addition, the claim 7 claimed "a purified and isolated DNA sequence……to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake."[262] Enhance production reticulocytes and hemoglobin synthesis involve the usage of the invention and this clearly support the requirement of useful in granting a patent. Lastly, claim 8 of the same patent stated "a cDNA sequence according to claim 7."[263] This can possibly infer that cDNA is a patentable invention.

Case 3- *Schering Corporation and Biogen v. Amgen Inc.*(2000)

Plaintiffs in this case, Schering Corporation and Biogen, Inc. sued the defendant, Amgen Inc. for patent infringement at district court for the District of Delaware.[264] The district court held defendant did not infringe plaintiff's patent, therefore, plaintiff appealed.[265] The patent in suit has U.S. Patent No. 4,530,901 ('901 patent) and the patent claims the recombinant DNA molecules encoding specific types of human interferon, microorganisms genetically engineered to produce the interferon and methods of producing interferon with recombinant technology.[266] The Federal Circuit

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[260] *Id.*
[261] *Id.* at 1204.
[262] *Id.*
[263] *Id.*
[264] Schering Corportation and Biogen, Inc., v. Amgen Inc., 222 F.3d 1347, 1347 (Fed.Cir. 2000).
[265] *Id.*
[266] *Id.* at 1348.

affirms the district court's judgment of non-infringement.[267]

Within '901 patent, the claim 1 of claimed "A recombinant DNA molecule consisting of segments of DNA from different genomes which have been joined end to end outside of living cells and which have the capacity to infect some host and to be maintained therein….comprising a DNA sequence selected from the group consisting of…"[268] and claim 5 states "A unicellular host transformed with at least one recombinant DNA molecule….comprising a DNA sequence selected from the group consisting of…"[269]. Both claims are composition claims that involve human intervention in transforming the host cells by joining different foreign genomes. Thus, this allows the host cells to have capacity to infect other cells and produce the desired protein products.[270] The new distinct characteristic that produces new proteins is the result of the transformation that resulted from human intervention by joining the original bacteria DNA sequence with foreign DNA sequence.[271] Patent invalidation based on the issue of non-patentable subject matter was not discussed in the case. Thus, this can lead to the possible inference that the invention that transformed by human intervention that produces a new product or desirable product is a patentable subject matter.

Case 4- *Genzyme Corp and Mount Sinai School of Medicine of New York University v. Transkaryotic Therapies, Inc.* (2004).

Patent owner of method of producing human enzyme, Genzyme Corporation and Mount Sinai School of Medicine sued their competitor, Transkaryotic Therapies, Inc., for patent infringement at District Court of District of Delaware and the case was later appealed to the Federal Circuit.[272] The patentee's patent number 5,356,804 regards to insertion of exogenous genes encoding enzyme of interest, <<alpha>>-Gal-A, into host cell's chromosomal material so the enzyme can be further expressed and secreted

[267] *Id.*
[268] *Id.* at 1350.
[269] *Id.*
[270] *Id.*
[271] *Id.*
[272] Genzyme Corporation and Mount Sinai School of Medicine of New York University v. Transkaryotic Therapies, Inc., 346 F.3d 1094, 1094 (Fed. Cir. 2004).

by the host cells[273]. The accused process involves insertion of promoters which activated endogenous genes encoding enzyme of interest.[274] The Federal Circuit holds that patentee's method was not infringed by the accused process patent.[275]

In a patent suit, infringement can only be sustained on the basis that the patent is valid. Thus, the holding of non-infringement by the Federal Circuit proved the validity of this gene patent. In the rationale of the case, the Court mentioned the context in column 14, lines 10-14 of the patent, mentioned transforming a host cell with a controllable DNA where "Host cells can be *transformed* with <<alpha>>-Gal-A or DNA controlled by appropriate expression control elements."[276] The validity of the patent is based on the insertion of a gene into host cell that *transforms* the host cell to perform the product of interest.[277] Hence, this shows the same standard as the precedent cases in determining the patentable subject matter; *transformation* is an essential character in distinguishing the human made invention from the natural product.

### 3.2.2 Determining the Patentability of Method or Process Claim for Gene Patent

Case 1- *Gottschalk v. Benson* (1972)

The patent application involves a method for converting binary coded decimal numerals into pure binary numerals for use with general purpose digital computer of any type.[278] Board of Appeals of the United Sates Patent Office affirmed with the decision.[279] At last, the Supreme Court held that computer program is a mathematical formula that is without substantial "practical application" except in connection with digital computer, therefore it cannot be a patentable process.[280]

The Court relied on the "physical transformation" requirement as numerous cases showed congruent perspective of this standard. In *Corning v. Burden*, the chemical or the physical acts that transform the raw material are sufficiently definite

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[273] *Id.*
[274] *Id.*
[275] *Id.*
[276] *Id.* at 1100.
[277] *Id.*
[278] Gottschalk v. Benson, 409 U.S. 63, 63 (1972)
[279] *Id.*
[280] *Id.*

to confine the patent monopoly.[281] In *Cochrane v. Deener*, the case involved a process for improving the manufacturing quality for flour.[282] The Court explicitly stated that "*transformation* and *reduction* of an article 'to a different state or thing' is the clue to the patentability of process claim that does not include particular machines.'"[283] In *Expanded Metal Co. v. Bradford*, involves a patentable process that expands metal and the Court declared that process patent "involves mechanical operations, and producing a new and useful result" and it should not limit to chemical actions.[284]

The Court declared process patent must undergo the examination that it be either tied to particular machine/apparatus or must operate to *change* articles/materials to a different state or thing.[285] The Court clearly stated it is leaving "no room" for the revelations of the new technology. However, if the judgment is affirmed then the patent would "wholly pre-empt" the mathematical formula and in practical effect would be a patent on the algorithm itself because the only possible use was on the digital computer.[286]

Case 2- *Parker v. Flook* (1978)

The case started from a rejection of claims for a "method for updating alarm limits" from Trademark Office Board of Appeals because the subject matter, the formula or algorithm, was already held unpatentable under *Benson*.[287] The patent in suit is a method that consist three steps: (1) measures the present value of the process variable (2) uses an algorithm to calculate an updated alarm limit value (3) is where actual alarm limit is adjusted to the updated value.[288] The only difference between the conventional methods of changing alarm limits and the patent application is regarding the second step of the patent in suit, algorithm.[289] This relates to one of the two issues in this case where whether post-solution applications of formula/algorithm would

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[281] Corning v. Burden, 56 U.S. 252, 253 (1853).
[282] Cochrane v. Deener, 94 U.S. 780, 780 (1876).
[283] Gottschalk v. Benson, 409 U.S. 63, 64 (1972).
[284] Expanded Metal Co. v. Bradford, 214 U.S. 366, 384 (1909).
[285] Gottschalk v. Benson, 409 U.S. 63, 71 (1972).
[286] *Id.*
[287] Parker v. Flook, 437 U.S. 584, 599 (1978).
[288] *Id.*
[289] *Id.*

make method eligible for patent protection.

The Supreme Court held (1) the finding of post-solution "applications for the formula" did not make the method eligible for the patent (2) the application provided a new and presumably a better method for calculating alarm limit values, where the only "novel feature" was the "mathematical formula or algorithm" and thus not a patentable subject matter.[290] Regarding the first issue, the Court explained a principle is a fundamental truth; an original cause; a motive those cannot be patented.[291] It was specifically point out that a process application use a principle in specific fashion then it will not automatically falls with the patentable subject matter otherwise the determination of patentable subject matter will only rely on the draftsman's art.[292] The discovery of law of nature cannot be patented is not because natural phenomena are not process but it is not the kind of "discovery" that statue was enacted to protect.[293] The second issue, the Court held patent application is not patentable under 35 U.S.C §101 because "once the algorithm was assumed to be within the prior art, the application, considered as a whole, contains no patentable invention."[294] The chemical process of converting the hydrocarbons are well known and limited, the use of alarm limits to trigger alarms and alarm limits are re-computed and re-adjusted so the patent application simply provides a new and presumably better method for calculating alarm limit values. The Court reaffirmed Court of Customs and Patent Appeals' reasoning that "if a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is non-statutory."[295] Therefore, by narrowing or limiting abstract idea to one field of use or adding post-solution components did not make the concept patentable.[296]

Case 3- *Diamond v. Diehr* (1981)

The case involves a patent application for process for producing cured synthetic

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[290] *Id.* at 584.
[291] Le Roy v. Tatham, 55 U.S. 156, 175 (1852).
[292] Parker v. Flook, 437 U.S. 584, 593 (1978).
[293] *Id.* at 593.
[294] *Id.* at 584.
[295] *In re* Richman, 563 F.2d 1026, 1030 (C.C.P.A. 1977).
[296] Parker v. Flook, 437 U.S. 584, 584 (1978).

rubber products.[297] The process took temperature measurement during cure and used a mathematical algorithm, Arrhenius equation to calculate the curing time. [298]Along the judgment, the Court stated that mathematical algorithm alone is not patentable because mathematical relationship is similar to a law of nature.[299]

However, the Court held that the claimed process an eligible patent subject matter because the inventors did not seek to patent a mathematical formula.[300] Instead they seek patent protection for a process of curing synthetic rubber.[301] Their process admittedly employs a well known mathematical equation, but they do not seek to pre-empt the use of that equation.[302] Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.[303] A clear difference between "seek to pre-empt the use of" fundamental principle and foreclose others from using "application of" fundamental principle. As the court stated "It is now commonplace that an application law of nature or mathematical formula to a known structure or process may well be deserving of patent protection. … Arrhenius' equation is not patentable in isolation, but when a process for curing rubber is devised which incorporates in it a more efficient solution of the equation, that process is at the very least not barred at the threshold by § 101."[304] If the claim allows the patentee to pre-empt substantially all uses of that fundamental principle, then it cannot be a patent eligible subject matter.[305] Therefore, in this case, the claims at issue did not pre-empt "all uses" of the Arrhenius equation but only "a process for curing rubber" and the process was claimed precisely, so it meets the qualification stated by the court. Thus, anyone would still be able to use the Arrhenius equation in any process not involving curing of rubber or any process to cure rubber that did not include performing all the "precisely stated steps in the claimed process."[306]

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297 Diamond v. Diehr, 450 U.S. 175, 177-79 (1981).
298 *Id.*
299 *Id.*
300 *Id.* at 187.
301 *Id.*
302 *Id.*
303 *Id.* at 176.
304 *Id.* at 187-88.
305 *Id.* at 203.
306 *Id.* at 175.

Also, prohibition against patenting abstract ideas "cannot be circumvented by attempting to limit the use of the formula to a particular technological environment" or adding "insignificant post-solution activity."[307] But the claim was not "an attempt to patent a mathematical formula, but rather was an industrial process for the molding of rubber products," so it qualifies the patentable subject matter.[308]

Case 4- *In re Bilski* (2008)

*In re Bilski* case involves a method of hedging risks in commodities trading.[309] An *en banc* decision was made from the United States Court of Appeals for the Federal Circuit (CAFC) on the patenting of method claims such as business methods.[310] The Federal Circuit court affirmed the rejection of the business method claims in suit.[311] The court proclaimed the machine-or-transformation test (hereinafter MOT test) as the applicable test for patent-eligible subject matter and that the "useful, concrete and tangible result" test[312] in *State Street Bank v. Signature Financial Group* should be abandoned.[313]

The MOT test was set up in this case for the standard for patent eligible process is if: (1) it is *tied to* a particular machine or apparatus, or (2) it *transforms* a particular article into a different state or thing. This Court concluded that machine or transformation test is the sole test for determining patent eligibility of a "process" under 35 U.S.C. §101. The applicant's claimed process does not "transform" any article to a different state or thing and they are not representative of physical objects or substances.[314] The process claimed encompass the exchange of only options which are only legal rights to purchase some commodity at a given price in a given time period.[315] The claim refers to the transaction that relates to the exchange of these legal rights at a "fixed rate corresponding to a risk position."[316]

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[307] *Id.* at 191.
[308] *Id.* at 175.
[309] *In re* Bilski, 545 F.3d 943, 943 (Fed. Cir. 2008).
[310] *Id.*
[311] *Id.*
[312] State Street Bank & Trust Co. v. Signature Financial Group, Inc., 149 F.3d 1368, 1373 (Fed. Cir. 1998).
[313] *In re* Bilski, 545 F.3d 943, 943 (Fed. Cir. 2008).
[314] *Id.* at 959.
[315] *Id.* at 947.
[316] *Id.* at 949.

The Court concluded that the claim was not drawn to patent eligible subject matter under the examination of the machine or transformation test. The case was then appealed to the Supreme Court as *Bilski v. Kappos*.

Case 5 - *Prometheus v. Mayo* (2009)

Prometheus is the sole and exclusive licensee of the two patents.[317] The patents claimed methods for calibrating the proper dosage of thiopurine drugs that are used for treating gastrointestinal and non-gastrointestinal autoimmune diseases.[318] The drugs are called 6-mercaptopurine (hereinafter 6-MP) and azathiopurine (hereinafter AZA).[319] When 6-MP is used to treat a patent, the body will break down 6-MP into various metabolites such as 6-methyl-mercaptopurine (hereinafter 6-MMP) and 6-thioguanie (hereinafter 6-TG) and nucleotides.[320]

The patents claim the measurements of these two metabolites as in indication of drug toxicity so therapeutic efficacy can be optimized. The measurement allows the determination of increasing and decreasing the level of drug to be administered thus to maximize the efficacy of treatment and minimize the toxicity of the drugs.

The Court in this case focused that the issue of patentability is whether a claim is drawn to a ”fundamental principle” or “an application of a fundamental principle.” In the case, *In re Bilski*, the “definitive test” for determining eligibility of a process patent under 35 U.S.C. §101 is the machine-or-transformation test.[321] The Court in this case further emphasized that the machine-or-transformation has two further aspects. The first aspect is “the use of a specific machine or transformation of an article must impose meaningful limits on the claim’s scope to impart patent-eligibility.”[322] The second aspect is “the involvement of the machine or transformation in the claimed process must not merely be insignificant extra solution activity.”[323] Thus the transformation must be central to the purpose of the claimed

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317 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d.1336, 1339 (Fed. Cir. 2009).
318 *Id.*
319 *Id.*
320 *Id.*
321 *In re* Bilski, 545 F.3d 943, 954 (Fed. Cir. 2008).
322 *Id.* at 961-62.
323 *Id.*

process.[324] Also, one cannot ground the transformative nature of a process in a step that is "insignificant extra-solution activity" or merely a "data-gathering step."[325] The Court concludes that methods of treatment claimed in the patents in suit qualify the patentable subject matter because the methods" transform an article into a different state or thing," and this transformation is "central to the purpose of the claimed process."[326] The transformation of the human body after the administration of the drug causes *chemical* and *physical changes* of the drug metabolites that allow the examiner to measure the concentrations.[327]

Case 6 – *Bilski v. Kappos* (2010)

Applicants appealed for the rejection of all claims by the Federal Circuit in which it affirmed with Board of Patent Appeal and Interferences decision that business method patent in suit cannot be eligible for the patentable subject matter.[328] The case was granted Certiorari.[329]

The Supreme Court affirmed with the CAFC's decision however provided with some different perspectives. For example, the Supreme Court rejected the MOT test as the sole test for determining eligibility of a process, even though MOT test may be useful and important as investigative tool.[330]

In the rationale of the Court, petitioners' application is not a patentable "process." Claims 1 and 4 included hedging or protecting against risk: "Hedging is a fundamental economic practice long prevalent in our system of commerce and taught in any introductory finance class."[331] The concept of hedging in claim1 and reduced to a mathematical formula in claim 4 is similar to the algorithms at issue in *Benson*[332] and *Flook*[333], therefore unpatentable abstract idea. The attempt to patent the use of the abstract idea in this case is similar to *Flook* by the "limiting" the field of use by

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[324] *Id.*
[325] *Id.* at 963.
[326] *Id.* at 962.
[327] Prometheus Lbs., Inc. v. Mayo Collaborative Servs., 581 F.3d. 1336, 1336 (Fed. Cir. 2009).
[328] Bilski v. Kappos, 130 S. Ct. 3218, 3220 (2010).
[329] *Id.*
[330] *Id.* at 3221.
[331] *In re* Bilski, 545 F.3d 943, 1013 (Fed. Cir. 2008).
[332] Gottschalk v. Benson, 409 U.S. 63, 63 (1972).
[333] Parker v. Flook, 437 U.S. 584, 584 (1978).

hedging risk in the energy market and then use analysis to input data into the equation. By allowing the patent application, it may risk to pre-empt use of this approach in all fields.

Case 7 – *Mayo v. Prometheus* (2012)

The case was appealed from the Federal Court and certiorari was granted. The case was remanded for reconsideration. On remand, the Court of Appeals, Lourie, Circuit Judge again reversed. Certiorari was granted. The Supreme Court, Justice Breyer, held that process patents claimed are law of nature, therefore, invalid.[334]

The court reached the ruling first on the determination of the machine or transformation test.[335] The claims purport to apply the natural laws describing the relationships between the concentrations in the blood of certain metabolite. The claimed processes have not transformed the unpatentable natural laws into patent eligible applications of those laws.[336] Also, based on the *Flook* and *Bilski* where the Court declared the insistence of a process that focuses upon the use of a natural law also contain other elements or a combination of elements, sometimes as referred to as an "inventive concept," sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.[337] The claims add nothing specific to the laws of nature other than what is well understood, routine, conventional activity.[338] The Court concluded that the process claims at issue invalid.[339]

### 3.3 Summary table 1 – Well Accepted Standard Prior to the *Myriad* case

[334] Mayo v. Prometheus, 132 S.Ct. 1289, 1299 (2012).
[335] *Id.*
[336] *Id.*
[337] Parker v. Flook, 437 U.S. 584, 594 (1978).
[338] Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 1299 (2012).
[339] *Id.*

| Issue / Case | Issue (1) – Law of nature, physical phenomena, and abstract ideas are three exceptions to 35 U.S.C §101 that cannot be granted a patent | Issue / Case | Issue (2) - Application of a law of nature or mathematical formula may deserve patent protection |
|---|---|---|---|
| 1.*Diamond v. Chakrabarty* (1980) | Congress intended statutory subject matter to "include anything under the sun that is made by man." Nevertheless, this is not to suggest that 35 U.S.C. §101 has no limits or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable. | 1.*Mackay Radio & Tel. Co. v. Radio Corp. of Am.* (1939) | The Court declared that while a scientific truth, or the mathematical expression of it, is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be. |
| 2.*Gottschalk v. Benson* (1972) | The Court clearly indicated that 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. | 2. *Funk Bros. Seed Co. v. Kalo Co.* (1948) | If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end. |
| 3.*Funk Brothers Seed Co. v. Kalo Inoculant Co.* (1948) | If the qualities of their invention are work of nature and discovery of the phenomena of nature are not patentable. The qualities of the bacteria claimed by the patent at issue are like the heat of the sun, electricity, or qualities of metals. The manifestation of laws of nature should be free to all men and reserved exclusively to none. | 3. *Diamond v. Diehr* (1981) | A claim drawn to a fundamental principle is not patentable, however, "an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." The new method for molding raw, uncured synthetic rubber into cured precision products, by using a "mathematical formula" may deserve patent protection. |

## 3.4 - Summary tables –Issues at Debate Prior to the *Myriad* Case

### 3.4.1 - Standard for Qualifying the Distinction between Product of Nature and Human-made Invention

| Issue / Case | Issue (1)(a) - Standard for qualifying the distinction between product of nature and human-made invention **-(*Natural Product in general )*** | Issue / Case | Issue (1)(b) - Standard for qualifying the distinction between product of nature and human-made invention **-(*Gene specific)*** |
|---|---|---|---|
| 1. *Hartranft v. Wiegmann* (1887) | The Court held the shells are still shells. They had not been manufactured into a new and different article, having a *distinctive name, character, or use* from that of a shell. The application of labor to an article, either by hand or by mechanism, does not make the article necessarily a manufactured article. | 1. *Diamond v. Chakrabarty* (1980) | The Supreme Court held that bacteria with markedly different characteristics from any found in nature and one having the potential for significant utility. Additionally, the court proclaimed the "'claim is not to a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter – a product of human ingenuity 'having a distinctive name, character and use.'" His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101 |
| 2.*Parke-Davis v. Mulford Co.* (1911) | Patent at suit is regarding isolation of a purified substance, adrenalin, from the suprarenal glands of animals. The Court held, the patent is only for a degree of purity and therefore it is not a new 'composition of matter,' but this cannot deny the invention as not patentable. Patentee was the first to make the invention has practical purpose a *new* thing commercially | *2. Amgen, Inc v. Chugai pharmaceutical co.* (1991) | Within the '195 patent, one of the claims stated that "a pharmaceutical composition for treatment of anemia comprising a therapeutically effective amount….a pharmaceutically acceptable vehicle." This same standard was used in *Parke-Davis v. Mulford Co.* case in determining a patentable invention. The invention of that case was granted patent based on the commercially and therapeutically effective result by the purified product. Thus, this |

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| | and therapeutically viable, which is a good ground for a patent. | | shows the same standard in distinguishing the natural product from the human made invention prior to evaluation of other elements of a patentable invention.<br>In patent'008, the claim 6 claimed that "a prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 5." This shows the transformation requirement to distinguishing the natural product and human made invention. Claim 7 of the same patent purported "a purified and isolated DNA sequence……to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin synthesis or iron uptake that involves the usage or utility of the invention. This can support the requirement of usefulness in deciding a patentable invention. cDNA composition claim was granted patent. |
| 3. *American Fruit Growers v. Brogdex Co.* (1931) | The addition of borax to natural fruit does not produce from the raw material an article for use which posses a new or distinctive form, quality or property. The addition of the boric compound only protects the natural fruit against deterioration by inhibiting development of the mold's spores. There is no change in the name, | 3. *Schering Corporation and Biogen v. Amgen Inc.*(2000) | '901 patent involves both composition claim and method claim as '901 patent claims recombinant DNA molecules encoding specific types of human interferon, microorganisms genetically engineered to produce that interferon, and methods of producing interferon with recombinant technology. Both claims are composition claims that involve human intervention in transforming the host cells |

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| | appearance or general character of the fruit. The fruit remains the same beneficial use. There must be transformation; a new and different article must emerge 'having a distinctive name, character, or use." | | by joining different foreign genomes. Thus, this allows the host cells to have capacity to infect other cells and produce the desired protein products. The new distinct characteristic that produces new proteins is the result of the transformation that resulted from human intervention by joining the original bacteria DNA sequence with foreign DNA sequence. Patent invalidation based on the issue of non-patentable subject matter was not discussed in the case. Thus, again reaffirms District Court and Federal Court's view of granting gene patents and whether the existence of transformation by human intervention may help to determine a patentable subject matter |
| 4. *Funk Bros. Seed Co. v. Kalo Co.* (1948) | No species acquires a different use. The combination of species produces no new bacteria, no change in six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect as it always had. The bacteria perform in their original natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee. | 4. *Genzyme Corp and Mount Sinai School of Medicine of New York University v. Transkaryotic Therapies, Inc.* (2004) | Patent number 5,356,804 regards to insertion of exogenous genes encoding enzyme of interest, <<alpha>>-Gal-A, into host cells' chromosomal material so the enzyme can be further expressed and secreted by the host cells. Whereas, the accused process involves insertion of promoters which activated endogenous genes encoding enzyme of interest. The holding from the Federal Court ruled that patentee's method was not infringed by the accused process patent<br>In the rationale of the case, the Court mentioned the context in column 14, lines 10-14 of the patent, mentioned transforming a host cell with a controllable |

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| | | | DNA where "Host cells can be transformed with <<alpha>>-Gal-A or DNA controlled by appropriate expression control elements." The validity of the patent is based on the insertion of a gene into host cell that *transforms* the host cell to perform the product of interest. Hence, this shows the same standard as the precedent cases in determining the patentable subject matter; transformation is an essential character in distinguishing the human made invention from the natural product. |
| 5.In re *Marden* (1998) | The Court in this case stated that, the purification of the vanadium brings about its ductility nonetheless, the ductility or malleability of vanadium is one of its inherent or natural characteristics and held not patentable | | |

## 3.4.2 – Standard for Determining the Patentability of Method or Process Claim in Gene Patent

| Issue / Case | Issue (2) - The patentability of method or process claim when granting a gene patent |
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| 1.*Gottschalk v. Benson* (1972) | Even though law of nature, physical phenomenon or abstract ideas cannot be granted patent protection, but, when it is used in an application then it may be protected. The Court examined for any substantial practical application except in |

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| | connection with a digital computer. Furthermore, examination of *transformation* and *reduction* of an article to different state or thing and whether it is tied to a particular machine/apparatus is a clue to patentability of process claim. Lastly, the possibility of pre-emption. In this case, the mathematical formula would *wholly pre-empt* because the only possible use was on the digital computer. The overbroad claim is not differ significantly from a claim that just said "apply the algorithm." |
| 2. *Parker v. Flook* (1978) | Patent in suit is related to method for updating alarm limits. The court focused on whether the claimed process as doing anything other than "providing an unpatentable formula for computing an updated alarm limit," because an application of formulas maybe patented. In connection, the Court examined whether the patenting of formula would wholly preempt all the use. The Court ruled the use of computers for 'automatic monitoring alarming; were all "well known," to the point where, putting the formula to the side, there was no "inventive concept" in the claimed application of the formula. In addition, the Court specifically pointed out that a process application use a principle in "specific fashion" will not automatically falls within the patentable subject matter. |
| 3. *Diamond v. Diehr* (1981) | The process claimed in the patent involves taking the temperature measurement during curing rubber. The mathematical algorithm, "Arrhenius" equation is used to calculate the curing time. The Court held process is an act or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing. The respondent's claims for transforming raw, uncured synthetic rubber into a different state or thing are eligible for patent protection. The second consideration lies where if the claim allows the patentee to *pre-empt substantially all uses* of that fundamental principle, then it cannot be a patent eligible subject matter. Therefore, since in this case, the claims at issue did not *pre-empt* "*all uses*" of the Arrhenius equation but only "a process for curing rubber" and the process claimed precisely, so it meets the qualification stated by the court. The Court added emphasis that prohibition against patenting abstract ideas "cannot be circumvented by attempting to limit the use of the formula to a particular technological environment" or adding "insignificant post-solution activity." The Court declared that the overall process patent eligible if there is the "additional |

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| | step" of the process integrated the equation into the process as a whole. The process patent at issue was held patentable due to the transformation of the process into an inventive application of the formula. |
| 4. *In re* Bilski (2008) | The case involves patenting a business method which hedges the risks in commodities trading. The court reiterated the MOT test as the applicable test for patent-eligible subject matter and that the "useful, concrete and tangible result" test in *State Street Bank v. Signature Financial Group* should no longer be relied upon. The Court concluded that this machine or transformation test is the sole test for determining patent eligibility of a "process" under §101. Supreme Court' made it clear that effective pre-emption of all applications of hedging even just within the limited area of consumable commodities is not allowed. |
| 5. *Prometheus v. Mayo* (2009) | The patents claim the measurements of these two metabolites as in indication of drug toxicity so therapeutic efficacy can be optimized. The Federal Court emphasized that the MOT test has two further aspects. The first aspect is "the use of a specific machine or *transformation* of an article must impose meaningful limits on the claim's scope to impart patent-eligibility." The second aspect is "the involvement of the machine or transformation in the claimed process must not merely be insignificant extra solution activity." Thus the *transformation* must be *central to the purpose* of the claimed process and cannot be a step that is "insignificant extra-solution activity" or merely a "data-gathering step." The Court concludes that methods of treatment claimed in the patents in suit qualify the patentable subject matter because the methods transformation of the human body after the administration of the drug causes *chemical* and p*hysical changes* of the drug metabolites that allow the examiner to measure the concentrations. |

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| 6. *Bilski v. Kappos* (2010) | Applicants appealed for the rejection of all claims by the Federal Circuit in *In re Bilski*. In this case, the Supreme Court rejected the MOT test as the sole test for determining eligibility of a process, even though MOT test may be useful and important investigative tool. The concept of hedging is similar to the algorithms at issue in *Benson* and *Flook*. Therefore, it is not patentable abstract idea. Also by "limiting" the field of use by hedging risk in the energy market and then use analysis to input data into the equation may risk *pre-empt use of* this approach in all fields. |
| 7. *Mayo v. Prometheus* (2012) | The Supreme Court held the process patents at issue were invalid due to failure to qualify the conditions that were setup by the precedents. The Court reached the final ruling by first using the MOT test. Then, the Court focuses upon the use of a natural law if it contains other elements or a combination of elements, referred to as an "inventive concept." The claims add nothing specific to the laws of nature other than what is well understood, routine, conventional activity. The administering and determining, combined with a correlative "wherein" clause, were not sufficiently transformative of what was otherwise a claim to a natural law. The Supreme Court finally held the process patents in suit invalid. |

### 3.5 Overall Summary

In summary, when an invention belongs to "laws of nature, natural phenomenon, and abstract ideas" then it should fall into the undisputed exceptions to the protection of 35 U.S.C §101. From the *Flook* case,[340] the Court has declared that these are not the inventions that the statute enacted to protect. However, the application of law of nature or mathematical formula may deserve patent protection. For example, in *Mackay Radio & Tel. Co. v. Radio Corp. of Am.* case, the Court declared that while a scientific truth, or the mathematical expression of it, is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be.[341]

Set aside the undisputed standard, one of the main attentions of this thesis focus on the controversy that still exist in granting the human gene patent. From the

[340] Parker-Davis & Co. v. H.K. Mulford Co., 189 F.95, 95 (S.D.N.Y. 1911).
[341] Mackay Radio & Tel. Co. v. Radio Corp. of Am., 306 U.S. 86, 86 (1939).

precedent cases, the argument still lies in the examination for standard for qualifying the distinction between product of nature and human-made invention. Whether the claimed invention as a whole, is sufficiently distinct in its fundamental characteristics from natural phenomena to possess the required "distinctive name, character and use" may assist in determining the "markedly different" standard used in the *Myriad* case.[342] However, different courts have dissimilar views in terms of the standard for qualifying the distinction between product of nature and human-made invention. The precedent of distinguishing natural product can be further divided into two categories: 1) natural product in general and 2) gene patent in specific.

The first category involves natural product in general. In *Hartranft v. Wiegmann*, the determination whether the shells are manufactured is the central issue in that case.[343] The defendant cleaned the shells by acid and ground off the inner layers by an emery wheel to show the bright color.[344] The Court in that case stated that in order to render the shells subject to duty as 'manufacture of shells,' something more must be done than simply remove the outer surface either by acids or mechanical means and the shells still retain their special form and character hence are could not be classified as manufacture of shells.[345] Change of character or function, chemical similarity and change of special form and character, all needs to accord to the nature of the invention, whether the product or invention displays of change in "inherent characters" and functions play an essential role in determining the standard that may lead to patentability.

In *American Fruit Growers v. Brogdex Co.,* the addition of borax caused no change in the name, appearance or general character of the fruit. The fruit remains the same beneficial use.[346] The Court announced in order to receive a grant of patent, there must be a *transformation*; a new and different article must emerge 'having a distinctive name, character, or use."[347] Furthermore, in *Funk Bros. Seed Co. v. Kalo Co.,* the combination of bacteria species produces no a new bacteria or no produce any changes in six species of bacteria, and also no enlargement of the range of their

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[342] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1342 (Fed. Cir. 2011).
[343] Hartranft v. Wiegmann, 121 U.S. 609, 609 (1887).
[344] *Id.*
[345] *Id.*
[346] American Fruit Growers v. Brogdex Co., 283 U.S. 1, 12 (1931).
[347] *Id.* at 13.

utility.[348] Each species has the same effect it always had.[349] The bacteria perform in their natural way therefore it unable to meet the qualification standard to patent grant.[350] *In re* Marden, the purification of the vanadium brings about its ductility.[351] Nonetheless, the ductility or malleability of vanadium is one of its inherent or natural characteristics so it is held as non-patentable subject matter.[352]

The second category includes gene patents in specific. In *Diamond v. Chakrabarty,* the Supreme Court held that bacteria as patentable subject matter because the "'claim is not to a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter – a product of human ingenuity 'having a distinctive name, character and use.'"[353] Another similar case, *Schering Corporation and Biogen v. Amgen Inc,* in one of the claims purported "A unicellular host transformed with at least one recombinant DNA molecule….comprising a DNA sequence selected from the group consisting of…" [354] This composition claim involves human intervention in transforming the host cells by joining different foreign genomes. Thus, this allows the host cells to have capacity to infect other cells and produce the desired protein products. Both cases showing, genes are well protected under the current patent law. Lastly, in *Genzyme Corp and Mount Sinai School of Medicine of New York University v. Transkaryotic Therapies, Inc.,* the patentee's patent number 5,356,804 regards to insertion of exogenous genes encoding enzyme of interest, <<alpha>>-Gal-A, into host cell's chromosomal material so the enzyme can be further expressed and secreted by the host cell.[355] Court mentioned the context in column 14, lines 10-14 of the patent, mentioned transforming a host cell with a controllable DNA where "host cells can be transformed with <<alpha>>-Gal-A or DNA controlled by appropriate expression control elements.[356] The validity of the patent is based on the insertion of a gene into host cell that *transforms* the host cell to

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[348] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).
[349] *Id.*
[350] *Id.*
[351] *In re* Marden, 47 F.2d 958, 958 (C.C.P.A. 1931).
[352] *Id.* at 1060.
[353] Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
[354] Schering Corportation and Biogen, Inc., v. Amgen Inc., 222 F.3d 1347, 1350 (Fed. Cir. 2000).
[355] Genzyme Corporation and Mount Sinai School of Medicine of New York University v. Transkaryotic Therapies, Inc., 346 F.3d 1094, 1094 (Fed. Cir. 2004).
[356] *Id.* at 1100.

perform the product of interest.[357] Hence, this shows the same standard as the precedent cases in determining the patentable subject matter.

Until now, the cases mentioned above all share a commonality that there must be change of inherent or natural character or even new usage to the product in order to establish the qualifying standard that distinguish product of nature and human made invention. As some courts put it, there must be a transformation from the natural product. However in *Parke Davis v Mulford*, the Court held a different view on the standard that distinguish between natural product and human made inventions because the Court announced that even if the inventions were merely an extracted product without change, there is no rule that such products are not patentable.[358] The issue of this patent dispute lies on a degree of purity of the product. Whether the degree of purity qualifies change in inherent characteristic is a question. But, the degree of purity does not involve change in inherent characters of the product because the only change is the pureness of the product. This judgment contradicts with the standard from previous cases because the transformation test prong is lacking. The Court held the change in purity does not make the invention unpatentable because the patentee was the first to make the invention with a practical purpose and a *new* thing that is commercially and therapeutically viable and this is a good ground for a patent. However, whether a product or invention is "commercially and therapeutically viable" maybe different with the "markedly different" mentioned in the *Myriad* case because a product may qualify the commercially and therapeutically viable standard and not be able to fulfill the markedly different standard. For example, the invention is a more purified product that leads to commercially and therapeutically viable result may not necessary involves change of characters or natural qualities. The change in purity did not change the inherent characteristics or transform it into different product with a new characteristic.

Also, in *Parke Davis v Mulford*, the Court used the structural similarity test to compare between patentee and defendant's product in order to establish the standard that distinguish between human invention and product of nature.[359] The Court declared the chemical distinction depends on structural association in known

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[357] *Id.*
[358] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (S.D.N.Y. 1911).
[359] *Id.* at 108.

proportion into molecules and not presence of atom, thus there is a difference between two products. This issue will be further discussed as to how the Federal Circuit decides on this issue in the most recent landmark case, *Association for Molecular Pathology v. U.S. Patent and Trademark office*.

As for granting a method or process patent, all Courts first focused on whether the patent at issue involves natural phenomenon, law of nature or abstract ideas because these are not patentable inventions. Nonetheless, application of these exceptions may deserve patent protection. The assessment on whether by granting process patent would wholly pre-empt all uses and the assessment of whether adding any insignificant post-solution activity also take place in preventing the possibility of preemption. In *Gottschalk v. Benson,* one of the most important considerations rests on whether mathematical formula would *wholly pre-empt other possible uses.*[360] If by granting the patent would pre-empt all other uses then patent will not be granted. Similar standard was used in *Parker v. Flook*[361] and *Diamond v. Diehr*[362] where the Court in both cases examines any possibility for pre-emption. Also, in *Diamond v. Diehr,* the Court held the claims at issue did not *pre-empt* "*all uses*" of the Arrhenius equation but only "a process for curing rubber" and the process claimed precisely, thus it meets the qualification to a patentable process. [363] Furthermore, the Court emphasized an application "inventive" and not simply by adding "apply it" in the claim, may help the invention to qualify the patentable subject matter.

Not only the preemption standard was used, the machine or transformation test was also used to assists the determination of the patentability of process patent. Such test focused on whether the invention is tied to an apparatus or a transformation and reduction to a different state or thing and this transformation is the central issue to the process claim. All cases cited above except *Parker v. Flook* used the existence of transformation to evaluate the patentability.[364] This may raise the question of the requirement on transformation test before granting a process patent.

Thus, the controversies lie as whether if the "machine –or-transformation" can be

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[360] Gottschalk v. Benson, 409 U.S. 63, 72 (1972).
[361] Parker v. Flook, 437 U.S. 584, 589 (1978).
[362] Diamond v. Diehr, 450 U.S. 175, 187 (1981).
[363] *Id.* at 203.
[364] Parker v. Flook, 437 U.S. 584, 584 (1978).

the sole test to determine the patentable subject matter. *In re* Bilski, the court reiterated the MOT test as the applicable test or the sole test for patent-eligible subject matter.[365] However, in *Bilski v. Kappos*, the Supreme Court rejected the MOT test as the sole test for determining eligibility of a process, even though MOT test may be useful and important as investigative tool in determining the patentability of process patent.[366]

Nevertheless, how does the Federal Court interpret or incorporate these standards in this important recent case will be analyzed in detail in later chapters.

# Chapter 4 – The *Myriad* Case

## 4.1- Background Information Related to the Case

### 4.1.1 Information on Myriad Genetics, Inc.

Since of the founding of the company in 1991, Myriad Genetics has been one of the leading molecular diagnostic companies that focus on developing and marketing novel predictive medicine, personalized medicine, and prognostic medicine tests.[367] All the molecular diagnostic tests and analysis are carried out in their own reference laboratories. The developing plan of the company adheres to the belief that there is a shift from treatment paradigm to a prevention paradigm. Therefore, by understanding the genetic basis of disease, the cause and risk assessment of developing the disease can be identified and use this information to enhance the treatment. Also, unveiling the genetic makeup of particular disease allows a possible discovery of specific cause of the disease and allows medical practitioners to deliver the optimal dosage of drugs. The company includes a number of proprietary technologies such as DNA, RNA, and protein analysis that assist further understanding the roles of genes and their related proteins in the progression of disease.[368] The company utilize this information for develop new molecular diagnostic test that can assess an individual's risk for

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[365] *In re* Bilski, 54 F.3d 943 (Fed. Cir. 2008).
[366] Bilski v. Kappos, 130 S. Ct. 3218, 3218 (2010).
[367] Peter D. Meldrum, *Preventing disease. Improving quality of life. Saving lives* (2011), http://files.shareholder.com/downloads/MYGN/1940710309x0x509346/D71AC0C3-FB2C-4B7B-9C3E-75D4441A57A0/Myriad-Genetics-Annual-Report-2011.pdf.
[368] *Id.*

developing disease later in life (predictive medicine), or evaluate a patient's risk of disease progression and disease recurrence (prognostic medicine).[369]

*Products and services* - The company offers nine commercial molecular diagnostic tests, including five predictive medicine tests, three personalized medicine tests, and one prognostic medicine test.[370] The company markets those tests through the sale force of approximately 350 people in the United States[371] and has established operations in Munich, Germany, and Zurich, Switzerland and market three of their tests through their own European sale force.[372] In addition, the company has also entered into marketing collaborations with other organizations in selected Latin American and Asian countries.[373]

*Molecular Diagnostic tests* - Molecular diagnostic tests are made to analyze genes and their mutations in order to assess individual's risk of developing particular disease and also be able to evaluate the recurrence of certain disease. Lastly, via these molecular tests, valuable information on measuring each individual exposure can be obtained and later used to adjust the dosage to the optimal amount. In some circumstances, diseases can be prevented and if not, delay the occurrence. The tenth molecular diagnostic test is a test for determining whether a mole is a benign or malignant melanoma which is a type of skin cancer. Myriad is hoping to lunch the tenth molecular diagnostic in the 2012 fiscal period.[374]

The nine commercial molecular diagnostic tests that the company offers in the United States are:

1. BRAC*Analysis*, predictive medicine test for hereditary breast and ovarian cancer[375];
2. COLARIS, predictive medicine test for hereditary colorectal and uterine

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[369] *Id.*
[370] *Id.*
[371] *Id.*
[372] *Id.*
[373] *Id.*
[374] *Id.*
[375] *Id.*

cancer[376];

3. COLARIS AP, predictive medicine test for hereditary colorectal cancer[377];
4. MELARIS, predictive medicine test for hereditary melanoma[378];
5. OnDose, personalized medicine test to measure chemotherapy exposure to 5-FU[379];
6. PANEXIA, predictive medicine test for pancreatic cancer[380];
7. PREZEON, personalized medicine test to asses PTEN status for disease progression and drug response[381];
8. Prolaris, prognostic medicine test for prostate cancer[382]; and
9. TheraGuide 5-FU, personalized medicine test for chemotherapy toxicity to 5-FU[383].

*Company Revenue* -The total revenue was $122.8 million and $233.3 million for the three and six months ended December 31, 2011, an increase of approximately 22% and 21% over revenues of $100.4 million and $192.3 million for the same periods in the prior year.[384] Overall, the revenue grew 11% from 362.6 million in fiscal 2010 to 402.1 million in fiscal 2011. One important note is that among the *86.4%* of the total revenue came from BRAC*Analysis* test which provides the comprehensive test analysis of the BRCA1 and BRCA2 genes.[385] The operating profit increased 17% to $157.8 million compared to $135.1 million the prior year.[386]

### 4.1.2 History of Patents in Suit

Starting in 1989, various European and American research laboratories involved in the International Breast Cancer Linkage Consortium until 1990, Mary-Claire King at the University of California, Berkeley published a paper related to breast cancer

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376 *Id.*
377 *Id.*
378 *Id.*
379 *Id.*
380 *Id.*
381 *Id.*
382 *Id.*
383 *Id.*
384 *Id.* at 17.
385 *Id.*
386 *Id.*

gene located on chromosome 17, this gene was later named as BRCA1.[387] Dr. Skolnick is a genetic researcher and founder of Myriad who suggested combing the Utah Mormon Genealogy with Utah Cancer Registry, where the program for mapping genes is created.[388] Dr. Skolnick and his team were supported by National Institutes of Health and local venture capital group.[389] The access to detailed family information and detailed genealogical records, Myriad was able to analyze the sequence of the DNA sequence which comprises the BRCA1 gene. After Myriad isolated BRCA1 gene, the company collaborated with numerous research groups such as the Hospital for Sick Children in Toronto, University of Pennsylvania, and University of Laval to start the research for BRCA2.[390] BRCA2 was identified on November, 1995[391] and on December 21, 1995, Myriad filed for patents on the BRCA2 both in U.S. and Europe.[392]

### 4.1.3 BRCA1 and BRCA2 tests offered by Myriad Genetics, Inc.

With the grant of both BRCA1 and BRCA2 patents by USPTO, two major types of testing are invented by Myriad for diagnostic of these genes.[393] The standard test is called" Comprehensive BRAC analysis" that consists of the full sequencing of the BRCA1/2 genes.[394] The second type of testing is called "BART analysis" which is the supplemental test to Comprehensive BRAC Analysis.[395] BART test is used to detect nearly all large rearrangement mutations in the BRCA1 and BRCA2 genes.[396] The Comprehensive test cost over $3000 dollars per test and nearly $600 for the BART test.[397]

### 4.1.4 Patents in Suit table

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387 Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 201 (S.D.N.Y. 2010).
388 *Id.*
389 *Id.*
390 *Id.*
391 *Id.* at 202.
392 *Id.*
393 *Id.* at 203.
394 *Id.*
395 *Id.*
396 *Id.*
397 *Id.*

| Patent number | Claims |
|---|---|
| 5,747,282 ("282") | (SEQ ID NO: 2 depict the amino acid sequence of the BRCA1 protein, and SEQ ID NO: 1 depicts the nucleotide sequence of the *BRCA1* DNA coding region.) |
| Claim 1 | An isolated DNA coding for BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2 |
| Claim 2 | The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID:1 |
| Claim 5 | An isolated DNA having at least 15 nucleotides of the DNA of claim 1. |
| Claim 6 | An isolated DNA having at least 15 nucleotides of the DNA of claim 2. |
| Claim 7 | 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 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 20 | A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in 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. |
| 5,837, 492 ("492") Claim 1 | 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. |
| Claim 6 | 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. |

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| Claim 7 | The isolated DNA molecule of claim 6, wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID cNO:1. |
| 5,693,473 ("473") Claim 1 | An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in Table 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. |
| 5,709,999 ("999") Claim 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 germ line alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1. |
| 5,710,001 ("001") Claim 1 | 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 the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA 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 consisting of BRCA1 gene from a non-tumor sample of said subject, BRCA1 RNA from said non-tumor sample and BRCA1 cDNA made from mRNA from said non-tumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said non-tumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample. |
| 5,753,441 ("441") Claim 1 | A method for screening germ line of a human subject for an alteration of a BRCA1 gene which comprises comparing germ line 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 germ line 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." |
| 6,033,857 ("857") Claim 1 | |
| | 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. |
| Claim 2 | A method for diagnosing a predisposition for breast cancer in a human subject which comprises |

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|---|---|
| | comparing the germ line sequence of the BRCA2 gene or the sequence of its mRNA, in a tissue sample from said subject with the germ line sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germ line sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer. |

## 4.2 - District Court's Decisions

The Plaintiffs Association for Molecular Pathology et al (collectively "Plaintiffs") is made up of numerous non-profit organizations, researchers and patients.[398] The defendants are United States Patent and Trademark Office ("USPTO") and Myriad which include both Myriad Genetics and Directors of the University of Utah Research Foundation.[399] During the mid to late 1990s, Dr. Kazazian and Ganguly were performing BRCA1 mutations through GDL at the University of Pennsylvania.[400] The diagnostic method that they used to detect BRCA1 mutations is different from Myriad, but it does involve the "BRCA1" DNA sequence itself.[401] Myriad offered Dr. Kazazian a collaborative license which only limited to single mutation test and four mutations test to allow for testing of Ashkenazi Jewish patients.[402] Later, cease and desist letters were sent to Dr. Kazazian and University of Pennsylvania.[403] On August 26, 1998 notice of infringement was given to Dr. Kazazian. Myriad sued the University of Pennsylvania in November 1998 for infringement of the patents in suit.[404] On June 10, 1999, Myriad also sent a letter to the University of Pennsylvania in order to seek assurances that Dr. Kazazian and the university will stop the gene testing.[405] However, during 1999 and 2000, Dr. Kazazian was informed that he is free to conduct test on BRCA1/2 if it is for the purpose of academic research.[406]

In May 1998, Myriad offered Dr. Ostrer a license agreement to perform

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398 *Id.* at 186.
399 *Id.*
400 *Id.* at 204.
401 *Id.*
402 *Id.* at 205.
403 *Id.*
404 *Id.*
405 *Id.*
406 *Id.*

BRCA1/2 test, nonetheless, the limitations to the agreement is similar to Dr. Kazazian's agreement.[407] Dr. Ostrer declined the offer. On September 15, 1998, Dr. Barbara Weber at the Cancer Genetics Network Project was given a letter from Myriad the existence of their patents on BRCA1/2. Thus, GDL at the University of Pennsylvania stopped conducting services for Dr. Weber.[408] In September 1999, Myriad requested Georgetown University to stop sending genetic samples to GDL.[409] In December 2000, Yale DNA Diagnostic Lab also received a cease and desist letter and in 2005, Dr. Matloff sought for permission for Yale to perform screening for mutations caused by large arrangements, but her request was denied. Therefore, the suit took place.[410]

The suit first took place at Southern District of New York, where the Plaintiffs moved for summary judgment and declare invalid fifteen claims (the "claims in suit" in seven patents (the "patents in suit") relating to the human BRCA1 and BRCA2 genes. Some of the plaintiffs in this case are patients that were unable to obtain funding for Myriad testing services because the insurance will not cover for testing cost for them. For example, the BART test is not covered by the insurance company unless they are qualified as "high risk patients" with the standard set forth by Myriad.[411]

The Plaintiffs assert that these patents are unlawful under each of (1) the Paten 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 because the patents cover products of nature, laws of nature and /or natural phenomena, and abstract ideas or basic human knowledge or thought. The defendants moved to dismiss the complaint for lack of subject matter jurisdiction, lack of personal jurisdiction and failure to state a claim.

The two main issues focus on whether isolated DNA can be a patentable subject matter and also, whether the method that analyzes the gene sequence can be patented. United States District Court at South District of New York held that (1) patents for

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407 *Id.*
408 *Id.*
409 *Id.*
410 *Id.*
411 *Id.*

isolated DNA containing breast cancer susceptibility genes were invalid[412], and (2) patents for methods of analyzing gene sequences were invalid.[413]

Issue 1 - In considering whether the patents in suit comply with 35 U.S.C. §101, the proper analysis requires determining (1) whether the claimed invention possesses utility; and (2) whether the claimed invention constitutes statutory subject matter and that is whether it belongs to a "process, machine, manufacture, or composition of matter, or any new and useful improvement thereof,"[414] or whether the claimed invention falls within the judicially created "products of nature" exception to patentable subject matter and also "laws of nature, natural phenomenon, and abstract ideas."[415]

The District Court emphasize on that the patentable subject matter must be "markedly different" from a product of nature and the appropriate 35 U.S.C. §101 inquiry is whether claimed invention "as a whole", is sufficiently distinct in its fundamental characteristics from natural phenomena to possess the required "*distinctive name, character and use*."[416] The defining characteristics between the isolated DNA and native DNA are both used to sequence specific targeting and protein coding therefore there is no difference "in kind" and hence, not "markedly different" from product of nature.[417] Furthermore, like the discovery of mutual non-inhibition in *Funk Brother*s case, the discovery of the effect of certain mutations in a particular gene are both simply the application of techniques well known to the skilled in the art, as a consequence, not product of invention.[418] District court also emphasized that DNAs are the "physical embodiment of information," and this information is not only in the claimed isolated DNA molecules.[419] The composition claims that are directed to isolated DNA sequence are held invalid.

Issue 2 – In *Bilski*, the Court stated that the application of law of nature or mathematical formula to known structure or process may deserve patent protection.[420]

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412 Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 229 (S.D.N.Y. 2010).
413 *Id.*
414 35 U.S.C. § 101 (2006).
415 Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
416 Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 228 (S.D.N.Y. 2010).
417 *Id.* at 191.
418 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 127 (1948).
419 Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 228 (S.D.N.Y. 2010).
420 *In re* Bilski, 54 F.3d 943, 943 (Fed. Cir. 2008).

The *In re Bilski* case set up the machine –or-transformation test to examine the eligibility of process patent under §101.[421] One of the prongs in the machine or transformation test requires transformations to new articles.[422] However, the claims covered "analyzing" or "comparing" DNA sequence by any method covered mental processes independent of any physical transformation.[423] Also, the Court clearly declared that the transformation in method claims would constitute simply "data gathering steps" that are not "central to the purpose" of the claimed process.[424]

The decision of the court regarding the method claim is that the plain and ordinary meaning of the terms "analyzing" or "comparing" are only abstract mental process of "comparing" or "analyzing" gene sequence, hence, invalid.[425]

Government in amicus curiae pointed out man engineered DNA molecules are patent eligible composition of matter because they do not occur in nature.[426] In contrast, the isolated and unmodified genomic DNAs caused by evolution are not patent eligible. The "magic microscope" test proposed by the government supported this standard by stating that if this imaginary microscope could focus the claimed DNA in the human body, then the claim covers unpatentable subject matter.[427] Thus, cDNA sequence engineered by man could not be focused by the magic microscope in human body, so it should be patent eligible.[428]

### 4.2.1 **Table – Amici Curiae in District Court's Decisions on Granting the Patent for Human DNA Sequences**

| **Amici curiae** | **Characteristic** | **Contentions** | **Agree/ Against** |
|---|---|---|---|
| 1. American Medical Association ,<br>2. American Society | Non- profit organization representing physicians and medical students | Patents in suit are directed to un-patentable natural phenomena that is in violation of article I, Section 8, Clause 8 of the Constitution and | Against |

[421] *Id.*
[422] *Id.*
[423] Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 235 (S.D.N.Y. 2010).
[424] *Id.* at 236.
[425] *Id.* at 185.
[426] *Id.* at 191.
[427] *Id.* at 199.
[428] *Id.*

| | | | |
|---|---|---|---|
| of Human Genetics,<br>3. American College of Obstetricians and Gynecologists,<br>4. American College of Embryology and<br>5. The Medical Society of the State of New York | throughout U.S. | 35 U.S.C. §101 | |
| 6. March of Dimes Foundation,.<br>7. Canavan Foundation,<br>8. Claire Altman Heine Foundation,<br>9. Breast Cancer Coalition,<br>10. Massachusetts Breast Cancer Coalition,<br>11. National Organization for Rare Disorders and National Tay-Sachs & Allied Disease Association | Non-profit organization (Research in improve treatment for numerous diseases such as breast cancer.) | These amici allege that Myriad's patents include natural phenomena and laws of nature therefore restrict the future research and scientific progress. | Against |
| 12. National Women's Health Network, | Non- profit organization (seeks to improve the | Contention that isolated DNA is product of nature therefore not patentable. The patents | Against |

| | | | |
|---|---|---|---|
| 13. Asian Communities for Reproductive Justice,<br>14. Center for Genetics and Society,<br>15. Generations Ahead, and<br>16. Pro-Choice Alliance for Responsible Research | health of women, promote reproductive justice, and encourage responsible use and governance of genetic, reproductive technologies.) | will stifle innovation and interfere with patient access to medical testing and treatment. | |
| 17. International Center for Technology Assessment,<br>18. Indigenous People Council on Biocolonialism,<br>19. Greenpeace, Inc and<br>20. Council for Responsible Genetics | Non-profit organization (assisting the public and policy makers how technology affects society, protection of genetic material for indigenous people, address global environmental problems and protect public interest) | Contention that patents in suit are product of nature and gene patents have negative impact on the public and indigenous people | Against |
| 21. Biotechnology Industry Organization | U.S. largest biotechnology trade association (represent over 1200 companies who do research and development of biotechnological healthcare, agricultural, environmental, and | Isolated DNA fall within the categories of patent-eligible subject matter and patents provide incentives for investment that promotes the advancement of science | Agree |

| | | | |
|---|---|---|---|
| | industrial products.) | | |
| 22. Boston Patent Law Association ("BPLA") | Non- profit association of attorneys and intellectual property professionals | Patents on gene related inventions promote innovation by protecting the process | Agree |
| 23. Rosetta Genomics, Inc,<br>24. George Mason University | -A molecular diagnostics company that provides diagnostic tests for cancer and patent owner of several isolated nucleic acid sequence.<br>-A public university that does cancer diagnostic research that are patented. | The question of patentability of human gene sequence should left to Congress to promote and not hinder the innovation. Also, patents in suit should be lawful under 35 U.S.C §101. | Agree |
| 25. BayBio,<br>26. Celera Corporation, and<br>27. The Coalition for 21st Century Medicine,<br>28. Genomic Health Inc.,<br>29. Target Discovery, Inc.<br>30. XDx, Inc | -Non-profit and independent association that represents more than 330 companies that perform research and development, cures and diagnostics.<br>-Manufacturer of diagnostic products.<br>-Represents some of the world's most innovative diagnostic companies.<br>- A life science company that enhances the quality of cancer treatment.<br>- A company that discovers, and uses protein to improve clinical diagnosis and | Patent exclusivity is required for the development of personalize medicine and patents in suit are eligible under the regulations set forth in 35 U.S.C. §101 | Agree |

| | | | |
|---|---|---|---|
| | management of diseases.<br>- A molecular diagnostics company that discovers, develop, commercialize non0invasive gene expression test | | |
| 30. Kenneth Chahine | Professor | Allege that the scope of the claims in suit sufficiently limited to avoid claiming products of nature and the isolated DNA and diagnostic process fulfills the patentable subject matter. | Agree |
| 31. Kevin E. Noonan | Patent attorney | Isolated human DNA constitutes patentable subject matter and the rejection of isolated human therapeutics will have negative impact on development of personalized medicine and scientific research | Agree |

The general trend from the amici curiae shows those who against patenting human gene sequence are due to public reasons such as improvement of treatment, health of woman, assist public and policy makers how technology affects society. On the opposition, those who agreed to the patentability of human gene sequence are mostly companies or manufacturer that involve with health related research such as cure and diagnostic development. This trend clearly illustrates that two conflicting proposals: protection of public interest against protection of private research

development.

4.3 - Federal Court's Earlier Decisions

In the first decision made by the Federal Court, there are only four major issues: (1) whether the only competitor with unequivocal intent to resume clinical diagnostic testing of DNA sequences has standing; (2) whether the composition claims covering isolated DNA sequences are direct to patent-eligible subject matter; (3) whether the method claims for comparing or analyzing isolated DNA sequences are not patentable; and (4) whether the method claim for screening potential cancer therapeutics via changes in cell growth rates is patentable.[429] The Court held only competitor with unequivocal intent to resume clinical diagnostic testing of DNA has standing to invoke declaratory judgment.[430] The composition claims covering isolated DNA sequence are patent-eligible subject matter.[431] As for method claims, the method claims for comparing or analyzing isolated DNA sequences are not patentable.[432] But, method claim for screening potential cancer therapeutics via changes in cell growth rates is patentable[433]. The parties petitioned for certiorari and the United States Supreme Court granted petition and vacated and remanded.[434]

4.4 - Federal Court's Decisions in the Recent Remanded *Myriad* Case

*Issues of the case*

There are six issues declared by the Federal Circuit in this case. The first issue is who has the standing for claiming the declaratory judgment. The second issue is whether the organization plaintiffs have standing to invoke declaratory judgment. The third issue is whether the composition claims covering isolated DNA sequences directed to patent-eligible subject matter. The fourth issue is whether cDNAs are eligible for patent. The fifth issue is whether or not the method claims for comparing

429 Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1329 (Fed. Cir. 2011).
430 *Id.*
431 *Id.*
432 *Id.*
433 *Id.*
434 *Id.*

or analyzing isolated DNA sequences are patentable. The sixth issue is whether or not the method claims for screening potential cancer therapeutics via change in cell growth rates are patentable.

### 4.4.1 Issue 1 –Who Has the Standing for Claiming the Declaratory Judgment?

Declaratory Judgment Act set forth in 28 U.S.C 2201 (a).[435] This Act focuses on the "existence of actual controversy" and "specific type of cases" listed under Article III of the U.S. Constitution.[436].In *MedImmune* case, the Supreme Court used all-the-circumstances test and has held that the dispute must be "definite and concrete, touching the legal relations of parties having adverse legal interests, real and substantial, and admit of specific relief through a decree of a conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts."[437] Therefore, "basically, the question in each case is whether the facts alleged under all the circumstances, show that there is a *substantial controversy*, between parties having *adverse legal interests*, o*f sufficient immediacy* and *reality* to warrant the issuance of a declaratory judgment."[438] All the circumstances tests provides three part examination for determining whether an action satisfy the justifiable Article III controversy. The three parts are: standing, ripeness and mootness.[439]

The main issue in this case deals with the first part, standing of examination.[440] Federal Circuit holds that only three plaintiffs allow an injury caused by "affirmative patent enforcement" traceable to Myriad; Drs. Kazazian, Ganguly and Ostrer.[441] Out of these three only Dr. Ostrer clearly alleges a "sufficiently real and imminent" injury because he asserts an intention to "actually and immediately" engage in allegedly

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[435] 28 U.S.C § 2201(a) (Supp. IV 2010) ("In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought …..any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.").

[436] Aetna Life Ins. v. Haworth, 300 U.S. 227, 239-40 (1937).

[437] MedImmune, Inc. v. Genetech, Inc., 549 U.S. 118, 126 (2007).

[438] *Id.*

[439] Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc., 527 F.3d 1278, 1291 (Fed. Cir. 2008).

[440] *Id.*

[441] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 10 (Fed. Cir. 2012).

infringing activities.[442] Myriad did demand a patent royalty from Dr. Ostrer based on his clinical BRCA research and also a collaborative license that seek the doctor to work with them.[443] Ostrer was also aware Myriad was asserting patent rights to other similar parties. These facts helped the Court to establish an "actual controversy" under the totality of circumstance standard.[444]

In this case, when Federal Circuit examined the existence of the adverse legal position between Myriad and Dr. Ostrer, the court focus on whether or not Dr. Ostrer can engage in BRCA genetic testing without infringing any valid claims.[445] As for controversy of sufficient reality and immediacy, Dr. Ostrer has the resources and expertise to "immediately" undertake clinical BRCA testing and have immediately begin such testing.[446] In contrast, Drs. Kazazian and Ganguly allege that they will "consider" resuming the BRCA testing.[447] The court emphasized these 'some day' intentions are insufficient to support an "actual or imminent" injury for standing.[448] Hence, Drs. Kazazian and Ganguly do not have standing.[449] Based on the assertion by Myriad, that time has extinguished the immediacy and reality of any controversy because patentee's ten year silence presumptively extinguishes any reasonable objective fear of suit.[450] But, the Court held that assertion of its patent rights will dissipate as market players and products change, however, this case is different because the relevant circumstances surrounding Myriad's assertion of its patent rights have not changed despite the passage of time.[451] Myriad active enforcement of its patent rights forced Dr. Ostrer and other researchers and institution to cease BRCA testing making the company the sole provider for this testing.[452] "An active enforcement of one's patent rights against others can maintain a real and immediate controversy despite the passage of time."[453]

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[442] *Id.*
[443] *Id.* at 11.
[444] *Id.* at 10.
[445] *Id.* at 14.
[446] *Id.*
[447] *Id.* at 11.
[448] *Id.*
[449] *Id.*
[450] *Id.* at 10.
[451] *Id.* at 12.
[452] *Id.*
[453] Micron Tech., Inc. v. Mosaid Techs., Inc., 518 F.3d 897, 901 (Fed. Cir. 2008).

The Federal Circuit concluded that even though they agree with the district court's decision on the issue of standing however, a narrower ground is needed.[454] District court should limit the jurisdictional holding to "affirmative acts" by the patentee directed at "specific" plaintiffs who have passed Supreme's Courts declaratory judgment requirements for an "adverse legal controversy" and sufficient "immediacy and reality."[455] In this case, Dr. Ostrer is the only plaintiff that qualifies these requirements.

### 4.4.2 Issue 2- Whether the Organization Plaintiffs Have Standing to Invoke Declaratory Judgment?

Federal Court in this remanded case has add emphasis that various organizational plaintiffs in this case were not the target of any enforcement action or offered license agreements by Myriad and did not prepare to undertake potentially infringing activities.[456] They suffered no injury and therefore lack standing to bring this action.[457]

### 4.4.3 Issue 3 - Whether or Not the Composition Claims Covering Isolated DNA Sequences Directed to Patent-eligible Subject Matter?

Federal Court pointed out that the district court has made a contrary conclusion of the Supreme Court precedent cases.[458] The first point was that the district court has misread all "products of nature" should be denied of patent protection unless fulfill the "markedly different" standard.[459] The second point regards to how the Court should focus on the differences between isolated and native DNAs and not their similarity.[460]

Myriad asserts isolated DNA does not exist in nature, and isolated DNA are unlike native DNA, can be used as primers and probes for diagnosing cancer.[461] In contrast, the plaintiffs assert that isolated DNA molecule fails to satisfy 35 U.S.C.

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[454] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 14 (Fed. Cir. 2012).
[455] *Id.*
[456] *Id.* at 14.
[457] *Id.*
[458] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1329 (Fed. Cir. 2011).
[459] *Id.* at 1349.
[460] *Id.*
[461] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 16 (Fed. Cir. 2012).

§101 because the claims cover natural phenomena and products of nature and composition of matter that is patent eligible must have a "distinctive name, character, and use" so it qualifies the "markedly different" element that is distinct from natural substance.[462] The isolated DNAs in this case retained the same nucleotide sequence as native DNAs therefore it is not "markedly different." Plaintiffs also assert that isolated DNA claims have pre-emptive effect which excludes others to work the DNA gene.[463]

One of the precedents, the Court in *Chakrabarty* held that a man-made, living microorganism as a patentable manufacture or composition of matter within the meaning of 35 U.S.C. §101.[464] The plasmids inserted into the bacteria enabled single bacteria to breakdown different components of crude oil.[465] The bacteria was held patentable subject matter because the "claim is not to a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter – a product of human ingenuity 'having a distinctive name, character and use.'"[466] Another precedent, *Funk Brothers* case involved mixing culture of nitrogen fixing bacteria into one product that is capable of inoculating a broader range of leguminous plants.[467] The Court held that the non-inhibitive qualities in the bacteria are "like the heat of the sun, electricity, or the qualities of metals," the "work of nature" and therefore, not patentable.[468]

The Federal Circuit in this case distinguished human made invention and product of nature by stating that even if combined or altered in a manner not found in nature. Nevertheless, the human interventions have made the invention "markedly different" or "distinctive" then it should be a patentable subject matter.[469] The DNA molecules are markedly different which have distinctive chemical identity and distinctive from the molecules in nature. For example, BRCA1 gene in its native state resides on chromosome 17 and it is composed of 80 million nucleotides whereas BRCA2 resides

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462 *Id.*
463 *Id.*
464 Diamond v. Chakrabarty, 447 U.S. 303, 307 (1980).
465 *Id.*
466 *Id.*
467 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 127 (1948).
468 *Id.* at 129.
469 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 18 (Fed. Cir. 2012).

on chromosome 13 and it is composed of 114 million nucleotides.[470] However, when isolated sequences are produced, the introns are cleaved from the native DNA sequences.[471] The resulting isolated BRCA1 gene and BRCA2 genes only consisted of 5,500 nucleotides, and 10,200 nucleotides respectively.[472] This makes the isolated sequences comprise a distinctive chemical identity from the native DNA. The chemical manipulation makes the molecule "markedly different" from that exist in the body.

In *Pake-Davis & Co. v. H.K. Mulford Co*, the purification of adrenaline made the invention "for every practical purpose a new thing commercially and therapeutically," as a result, the Court held the purified adrenaline to be patentable subject matter.[473] In contrast, in *In re* Marden, the purified uranium is "inherently" ductile in purified form which indicate uranium was naturally ductile substance thus not a patentable subject matter.[474] In this case, when isolated DNAs are covalently bonded to other substance in its' natural form, so the DNA was chemically cleaved from the chemical combination with other genetic materials to produce the isolated DNA gene.[475] Hence it is not a purified form of natural material, but a distinct chemical entity.[476]

The plaintiffs assert that the isolated DNA sequences and native DNAs have same nucleotide sequences, so they do not satisfy the markedly different standard.[477] The Court answered the distinctive nature should used to evaluate the isolated composition of matter and not on the physiological use or benefit.[478] In addition, the eligibility of isolated gene should not be negated by having similar informational properties to more complex natural material that embodies it. The information content in this case is irrelevant to make the isolated gene eligible for patent. Isolated DNAs including cDNAs are markedly different chemical structure compared to their natural form, thus, qualify as patentable subject matter.

Federal Circuit expressed its opinion on the magic microscope test proposed

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[470] *Id.*
[471] *Id.*
[472] *Id.*
[473] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95 (S.D.N.Y. 1911).
[474] *In re* Marden, 47 F.2d 958 (C.C.P.A. 1931)
[475] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 19 (Fed. Cir. 2012).
[476] *Id.*
[477] *Id.*
[478] *Id.*

by the government. The Court announced that this test cannot be accepted because "it misunderstands the difference between science and invention. This test also fails to take into the existence of molecules as separate chemical entities." To be able to view DNA molecules via microscope is different from possessing a concrete form of nature that can be used to reduce to practice. As this Court clearly declared that, "visualization does not cleave and isolate the particular DNA; that is the act of human invention."

The Court concluded that granting this composition patent on DNA sequences comports with the longstanding practice of the USPTO and the Utility Examination Guidelines in 2001[479] reaffirmed their perspective on issue of the isolated DNA molecule.

### 4.4.4 Issue 4 –Whether or Not the cDNAs Are Eligible for Patent?

The cDNAs are categorized as one type of composition claim. Based on the previous discussion of the Federal Court on the ruling of another type of isolated DNA, the Court reached the decision based on the chemical distinctiveness of the invention. The chemical distinction is built on the "markedly different" chemical structure compare to the natural form. The cDNAs are distinctive, lacking the non-coding introns present in naturally occurring chromosomal DNA.[480] They are "even more the result of human intervention into nature and is hence patent-eligible subject matter".[481]

### 4.4.5 Issue 5 -Whether or Not the Method Claims for Comparing or Analyzing Isolated DNA Sequences Are Patentable?

Concerning the patentability of method claims that involves comparing or analyzing isolated DNA, the Court held the method of "comparing" or "analyzing"

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[479] In 2000, the PTO issued the Revised Interim Utility Guidelines Training Materials to provide patent examiners with guidance in assessing the utility requirement of section 101. The Training Materials provide that: (1) for method claims that recite more than one utility, if at least one utility is credible, specific, and substantial, a rejection under 35 U.S.C. § 101 should not be made, and (2) for product claims that do not recite any utilities, disclosure or assertion of one specific, substantial and credible utility meets the criteria of 35 U.S.C. § 101. Each of "credible," "specific," and "substantial" term is clearly defined.

[480] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 17 (Fed. Cir. 2012).

[481] *Id.*

BRCA sequences do not satisfy the MOT test in which the same test was applied in the *Prometheus* case. Myriad's methods claims included a transformation where first DNAs are extracted then transformed into properly sequence that allows the sequencing to take place.[482] Myriad asserts that the lower court misconstrue the term "sequence" because it does not represent information but a physical molecule[483] and district court has erroneously held the transformations in their patent are simply data-gathering steps rather than central to the purpose of the claims.

On the contrary, plaintiffs claim that the method claims are abstract idea and the claims to have a pre-emptive effect on the phenomenon of nature.[484] Alike previous precedents, by adding specific to limitation claims' application will not make the claims patent eligible.[485] Furthermore, the plaintiffs assert the claims do not meet the MOT test because it only include one step of "comparing" or "analyzing" the two DNA sequences.[486]

After the Federal Circuit renewed the claims of "comparing" or "analyzing," the Court still hold the method claims at issue are not patentable subject matter because the claims involves abstract mental processes.[487] In *Benson*, the Court held "phenomena of nature…mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work."[488] The comparison between tumor sequence in the research data base and patients' sequence shows genetic changes in the tumor sample and this is nothing more than an abstract mental step to compare two gene sequences.

The Supreme Court in *Bilski v. Kappos* held, "the prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula to a particular technological environment.'"[489] Similar view is shared in *Flook*, the Court held limiting an abstract idea to one field of use…did not make the concept patentable subject matter.

Myriad asserts that method claims are transformative and central to the purpose

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[482] Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1355 (Fed. Cir. 2011).
[483] *Id.*
[484] *Id.*
[485] *Id.*
[486] *Id.*
[487] *Id.* at 1356.
[488] Gottschalk v. Benson, 409 U.S. 63, 67 (1972).
[489] Bilski v. Kappos, 130 S.Ct. 3218, 3230 (2010).

of the claims. Myriad's argument is based on the Federal Court's holding of *Prometheus* case. In this case, claimed methods included steps of (a) "administering" a thiopurine drug to a subject, and/or (b) "determining" the drug's metabolites levels in the subject where metabolite levels are measured to optimize the drug dosage. The Court in that case held "administering" step and the "determining" step both transformative and central to the purpose of the claims because the metabolite levels could not be determined by only inspection and the "determining" step transformation occurred when metabolites are extracted from body sample and then determine their concentration. This fulfills the central purpose of the claims because it allows the optimization of drug dosage and not insignificant extra-solution activity. However, the method claims at issue were invalidated by the Supreme Court based on not qualifying the transformative prong in the MOT test. Using a similar analogy, Myriad's claims do not include "determining" the sequence of BRCA genes but only comparison of genes sequences, therefore, failed the MOT test. The Court also announced that the claims do not include extraction and sequencing of genes before comparing the two genes and neither comparing nor analyzing means or implies "extracting" or "sequencing" DNA.

Another of Myriad's assertion focused on the claim term "sequence" refers not to information but rather to a physical DNA molecule. However, Federal Circuit disagree with this argument because "sequence" does not exclusively specify a DNA molecule but refers more broadly to the linear sequence of nucleotide bases of a DNA molecule. The Federal Court declared this type of method claims is indistinguishable from the claims in *Mayo*. The Supreme Court invalidated the method claims in *Mayo* due to insufficiently transformative. The Federal Court in this case clearly announced the Supreme Court's holding of the *Mayo* case governs Myriad's these method claims at issue.

The Court held method claims of analyzing and comparing are abstract mental processes of comparing two gene sequences thus, fail to be a patentable subject matter.

### 4.4.6 Issue 6 – Whether or Not the Method Claim for Screening Potential Cancer Therapeutics via Change in Cell Growth Rates Are Patentable?

Plaintiffs' claims that Myriad's method for screening potential cancer

therapeutics via changes in cell growth rate is claimed in '282 patent claim 20 is an abstract idea and pre-empt a basic scientific principle.

In the rationale of the Court, it stated that claim includes transformative steps that include (1) "growing" host cells transformed with an altered BRCA1 gene in the presence or absence of potential cancer therapeutic (2)"determining" the growth rate of the host cells with or without the potential therapeutic and (3) "comparing" the growth rate of the host cells. The claim involves "growing" transformed cells that are like the patent eligible cells in *Chakrabarty*. The presence or absence of a potential cancer therapeutic that are inherently transformative step that relate to manipulations of cells and their growth medium. The claim also involves physical manipulation of cell where cells' growth rates are "determined". This fits the "central to the purpose" standard set up in *Prometheus*. Therefore, assess compound's potential as a cancer therapeutic, and growing of cells and growing rate work towards the same central purpose. The Federal Court in this case explained Supreme Court invalidated the claims in *Mayo* because of insufficient to differentiate the claimed method from the natural laws in the claims. Laws of nature are not patentable but the application of such law may deserve patent protection. But, the application of the law must fit the standard that it must do more than simply stating the law and adding the words 'apply it'.[490] The method claims in *Mayo* included additional steps but those steps were not sufficient to "transform" the mere expression of natural laws to patent eligible subject matter. But this is not the case here because the claim here is based on a man-made, non-naturally occurring transformed cell that is patent eligible subject matter.

The last consideration on the pre-emption of a scientific principle, this Court held that claim does not cover all cells, all compounds, or all methods of determining the therapeutic effect of a compound. The "specific host cells" transformed with "specific genes "are grown in the presence or absence of a specific type of therapeutic. This therapeutic effect is dependant solely on the cells' growth rate which do not pre-empt all uses of the natural correlations. Hence, the Court held this claim patentable subject matter.

## 4.5 - Concurring and Dissenting Opinions

[490] Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 1294 (2012).

(1) Judge Kimberly Moore concur-in-part but she wrote separately in terms of her reasoning. She first explained the congress did not limit the scope of patentable subject matter, however, the previous precedents did provided three firm exceptions to §101 broad patent-eligibility principles; 'law of nature, physical phenomena, and abstract ideas.'"[491] These thee exceptions " rest not on the notion that natural phenomena are not process but rather on the more fundamental understanding that they are not the kind of 'discoveries that the statute was enacted to protect." [492] Several cases regarding law of nature exception were introduce (please refer to the above for the summary of each case). She explained the courts have long applied the principles articulated in *Funk Brother* and *Chakrabarty* to determine if the invention at issue falls into the laws of nature exception and she comports with this longstanding flexible approach.

Further in her reasoning, she divides the issue of composition claims into two subcategories: (1) cDNA molecules that are different from the naturally occurring gene sequences and (2) isolated sequence claims that are identical to naturally occurring gene sequences. Moreover, she divided the isolated gene claims into two subcategories: short and long isolated gene sequences.

In general, on the issue of isolated sequence claims, Judge Moore does not agree with majority's opinion on deciding the eligibility of isolated DNAs solely based on chemical structure alone. She clearly explained the plain language of the statute requires that an invention be "new and useful."[493] Therefore, although the disputed DNAs qualify the determination of "changes in chemical identify," the "difference" must also impart a "new utility" that makes the molecules "markedly different" from nature.

In the rationale, the disputed cDNAs are held to be not part of laws of nature exception because cDNAs do not exist in nature. In addition, the cDNAs are made from RNA with a complementary relationship and they do not include non protein expressing introns. She emphasized the cDNAs only contain the coding nucleotides that are used to express proteins so they are different molecules from the natural RNA.

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[491] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).
[492] Parker v. Flook, 437 U.S. 584, 593 (1978).
[493] 35 U.S.C. §101 (2006).

Therefore, cDNAs do have a *distinctive name, character* and *use* that are associated with *markedly different* chemical characteristics. These help to distinguish from naturally found genetic material.

In terms of the short isolated DNA sequences, she tried to support her decision of granting composition patent by indicating the "new and distinct" characteristics compared to the sequences that occur in nature. For example, isolated DNA sequences have truncations with different ends and they can also be used as probes or primers that do not occur in natural DNA. The ability for the "use" of the isolated gene sequence is an "enlargement of the range of….utility" compare to nature.[494] This new application comes from physical properties of existing gene sequence. The new and significant utility is a product of the intervention of man and hence, the claimed cDNAs are patentable subject matters.

As for long isolated gene sequence, they are unlike the short gene sequence that can be used as primers or probes. Thus, the long isolated full gene does not clearly have a new utility but only act as gene encoding protein sequence. She pointed out if she can decide this case on a blank canvas; she might conclude the long isolated DNA sequence as non-patentable subject matter. But this is not the case, thus, she supported her decision of the patentability of long gene sequence based on the long standing practice of courts validating and USPTO granting gene patents.

In the past, the United States Patent Office has allowed thousands of isolated DNA sequence patents for decades and allowed purified natural products patents for centuries. For example, *Amgen, Inc. v. Chugai Pharmaceutical Co*., the Court in that case held the claimed invention "purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.'"[495] Thus, "disturbing the biotechnology industry's settled expectations may risk impeding, not promoting, innovation because those companies who relied on the reasonable decision to invest large amounts of time and money into the gene research may be disrupted."[496] Hence, changes are better to come from Congress as it is obviously aware of the issues presented in this case. " The subject matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting

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494 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).
495 Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1204 (Fed. Cir. 1991).
496 *Id.*

'the Progress of Science and the useful Arts'…"[497] Hence, the judicial power include "taking the statutes as we find them..."[498] "Our task.. is the narrow one of determining what Congress meant by the words it used in the statute; once that is done our powers are exhausted."[499]

(2) Judge William C. Bryson concurs with the judgment on standing, patentability on cDNA claims and method claims but he dissents on the subject of the composition claims for isolated gene sequence.[500]

In Judge Bryson's view, the isolated genes are not materially different from the native genes, thus should not be granted patent protection.[501] He explained "merely isolating the products of nature by extracting them from their natural location and making those alterations attendant to their extraction does not give the extractor the right to patent the products themselves."[502] The composition claims at issue claim the genes that appear in nature on the chromosome of living human beings.[503] He criticized the majority ruling of isolated genes as new molecules based on cleaving the bonds to when isolating those genes. In his view, a chemical bond is merely a force between two atoms or groups of atoms.[504] There is no magic to a chemical bond when the atomic or molecular forces are altered.[505] "A dirty diamond is cleaned with water or another solvent but that does not make the clean diamond a human made invention."[506]

Judge Bryson further supported his opinion by providing different examples of composition claims in his rationale: the short and the long isolated gene sequence. One of the short isolated gene sequence claims, claim 5 of the '282 patent, in Judge Bryson's opinion, has a breathtaking broad patent scope as it is likely be in any "sub-sequence" or part of other long genes.[507] Another example, the long isolated sequence in one of '282 patent claims, purported a sequence that is 24,000 nucleotides

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497 *Id.*
498 Diamond v. Chakrabarty, 447 U.S. 303, 315 (1980).
499 *Id.*
500 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 38 (Fed. Cir. 2012).
501 *Id.*
502 *Id.* at 40.
503 *Id.*
504 *Id.*
505 *Id.*
506 Am. Fruit Growers, Inc. v. Brogdex Co., 283 U.S. 1, 12 (1931).
507 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 45 (Fed. Cir. 2012).

long with numerous gaps denoted "vvvvvvvvvvvvv," and this means the claim is not defined by any particular chemical formula, therefore have incalculably large number of new molecules could be created by filling in those gaps.[508] This results with a very broad claim as well. These broad claims may present a significant obstacle to future innovation in genetic medicine such as multiplex tests and whole genome sequencing.[509]

In conclusion, based on the isolated gene sequence are those genes found in nature because breaking the chemical bonds do not turn those genes into "different materials", thus not patentable.[510] Moreover, the non-patentability of isolated gene sequence is supported by the possible stifling effect on future research and innovation when granting composition claims.

## 4.6 - The Comparison between the Two Federal Court Decisions

### 4.6.1 Majority's Opinion on the Issue of Invoking Declaratory Judgment Standing

The Federal Court reaffirmed the previous decision on the standing of invoking the declaratory judgment.[511] One small difference is the Court in this new case has divided the issue of standing into two smaller issues. The Court in this new case clearly indicated the various organizational plaintiffs in this suite lacked standing to invoke declaratory judgment because they were not the target of enforcement actions did not receive offer of license agreements by Myriad.[512] Furthermore, the organizational plaintiffs do not have any preparation to undertake the potentially infringing activities.[513]

### 4.6.2 Majority's Opinion on the Issue of Composition Claims - Isolated DNA Molecules

Focusing on the composition claims, the Federal Court reaffirmed the previous

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[508] *Id.*
[509] *Id.* at 46.
[510] *Id.* at 40.
[511] *Id.* at 1.
[512] *Id.* at 14.
[513] *Id.*

conclusion as well but it has further divided the composition claim into two more detailed issues: 1) composition claims covering isolated DNA sequences associated with predisposition to breast and ovarian cancers and 2) cDNA sequences which lacked non-coding introns.[514] In consideration of the *Mayo* case, the Federal Court in this case expressed *Mayo* does not control the question of patent eligibility of such claims because the claim at issue in the *Mayo* case was method claim and not composition claim.[515] But *Mayo* and earlier decisions concerning method claim patentability provide valuable insights. The Supreme Court's decisions in *Chakrabarty* and *Funk Brothers* were mentioned to set up the primary framework for deciding the patent eligibility of composition of matter.[516]

Regard to the issue of the first type of composition claim, the Court reaffirmed the previous decision based on a tangible, man-made composition of matter defined and distinguished by its objectively discernible chemical structure.[517] The markedly different chemical structure was supported by the difference in overall gene length. In addition, the isolated DNA is removed from its native and chromosomal environment by cleaving the covalent bonds, thus, a chemically manipulated entity.[518]

On the issue of the composition claim on the isolated cDNAs have markedly different chemical structure compared to native DNAs.[519] The remand of this case for reconsideration in light of *Mayo* suggests the composition claims are more than any product of man. Also permitting patents on a particular subject matter would prevent use by others, in *Mayo*, the correlation recited in the method claims.[520] But, the Court explained permitting patents on isolated genes does not preempt a law of nature.[521] A "composition of matter" is not a "law of nature."[522] Judge Lourie further explained everything and everyone comes from nature, following its laws.[523] But the compositions here are not natural products.[524] "They are the products of man albeit

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[514] *Id.* at 16.
[515] *Id.* at 15.
[516] *Id.* at 17.
[517] *Id.* at 20.
[518] *Id.*
[519] *Id.* at 31.
[520] *Id.* at 20.
[521] *Id.*
[522] *Id.* at 19.
[523] *Id.* at 21.
[524] *Id.*

that all materials do, laws of nature".[525] Snapping a leaf from a tree is a physical separation easily done by anyone.[526] Creating a new chemical entity is the work of human transformation, require skill, knowledge, and effort.[527]

### 4.6.3 Majority's Opinion on the Issue of Method Claims

In light of considering the Supreme Court's decision in *Mayo*[528], the Federal Court reaffirms the prior holding on method claims.[529] As for the first type of method claim that involve "comparing" or "analyzing" two gene sequences, the Court held the claim only include abstract mental process[530] and phenomena of nature ….mental process, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.[531] The Court explained "the claim recites nothing more than the abstract mental steps necessary to compare two different nucleotide sequences"[532] and "the comparison between the two sequences can be accomplished by mere inspection alone." [533] Furthermore, the Court emphasized that the Myriad other claims do not include a *Mayo*-like step of "determining" that involve transformative step.[534]

For the second type of method claim that recite screening for potential cancer therapeutics, the Court elucidate that "Supreme Court in *Mayo* invalidated the method patent in suit because in order to transform an unpatentable law of nature into a patent-eligible application of such a law, one must do more than state the law of nature and adding the words apply it."[535] In comparison, the existence of the transformed cells is more than simply apply a law of nature because the transformed cells are product of man and not of nature.[536] Moreover, "the claims does not cover all cells, all compounds or all methods of determining the therapeutic effect of a

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[525] *Id.*
[526] *Id.*
[527] *Id.*
[528] Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 1289 (2012).
[529] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 23 (Fed. Cir. 2012).
[530] *Id.*
[531] Gottschalk v. Benson, 409 U.S. 67 (1972).
[532] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 27 (Fed. Cir. 2012).
[533] *Id.* at 25.
[534] *Id.*
[535] *Id.* at 26.
[536] *Id.*

compound but it is tied to specific host cells transformed with specific genes."[537] Thus, the Federal Court held this type of method claim patent-eligible subject matter.[538]

### 4.6.4 Comparison of Judge Moore's Opinion

In the new remanded case, Judge Moore did not change any of her decisions.[539] She joined the majority opinion regarding to standing and the patentability of the method claims.[540] As for one type isolated DNA, cDNAs, she agreed with the majority opinion.[541] However, she provided a different reasoning on the second type of isolated DNA, which is the DNA that has same nucleotide sequence as the natural form.[542]

In her reasoning, the first part included the comparison of the court's decision on *Funk Brothers*[543] and *Chakrabarty*[544] and the exceptions to §101. This was identical with the decision of the previous cases. The second part mentioned that even though this case was remanded from the Supreme Court in light of its opinion in *Mayo Collaborative Services v. Prometheus Laboratories, Inc*.,[545] but she declared that the *Prometheus* decision does not control the outcome in this case.[546] The framework of *Funk Brothers* and *Chakrabarty* combining with the direction of *Prometheu*s, the applicable principles include: (1) laws of nature/manifestations of nature are not patentable; (2) a composition of matter with "markedly different characteristics" from that found in nature with the potential for significant utility is directed to patentable subject matter.[547] cDNA sequence has introns removed and it is the complementary sequence of nucleotides; thus, it does not exist in nature and therefore not fall within the "laws of nature" exception.[548] It is further emphasized that cDNA has different

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[537] *Id.*
[538] *Id.* at 27.
[539] *Id.*
[540] *Id.*
[541] *Id.*
[542] *Id.*
[543] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 127 (1948).
[544] Diamond v. Chakrabarty, 447 U.S. 303, 303 (1980).
[545] Mayo v. Prometheus, 132 S.Ct. 1289, 1289 (2012).
[546] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 31 (Fed. Cir. 2012).
[547] *Id.*
[548] *Id.*

chemical structure than RNA and it also provide a greater stability.[549] cDNA sequence has a distinctive character and use, with markedly different chemical characteristics from natural DNA or RNA.[550] In conclusion, the cDNA is not only within laws of nature exception but also possess markedly different characteristics. Therefore, cDNA should qualify as a patentable subject matter.

The majority held the second type of isolated gene, gene that has same nucleotide sequence, as the patentable subject matter based solely on the chemical differences.[551] But Judge Moore does not agree with majority's opinion on this issue. In her opinion, she first divided the isolated nucleotide sequence into long and short strands.

For the short isolated gene, Judge Moore viewed it as a different molecule because it has truncations (with different ends) that are produced with the intervention of man.[552] The smaller isolated DNA sequences can be used as the basis for probes that natural DNA cannot do because natural occurring DNA do not have the requisite chemical and physical properties needed to perform such function.[553] This ability is clearly an "enlargement of the range of …utility" compared to nature.[554] Judge Moore pointed out a difference between this case and *Prometheus*[555]. The difference is that in *Prometheus*, the claims at issue were only "set forth laws of nature – namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm."[556] The claimed relationship was "a consequence of the ways in which thiopurine compounds are metabolized by the body – entirely natural processes."[557] The ability to use the isolated DNA as a primer or probe to determine the mutation is a new and important utility substantially different from the role of DNA that occurs in nature.[558] Judge Moore reached the conclusion that short isolated DNA sequence is an alteration

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549 *Id.*
550 *Id.*
551 *Id.*
552 *Id.*
553 *Id.*
554 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).
555 Mayo v. Prometheus, 132 S.Ct. 1289, 1296-97 (2012).
556 *Id.*
557 *Id.* at 1297.
558 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 32 (Fed. Cir. 2012).

of the natural product with "markedly different characteristics from any found in nature and one having the potential for significant utility."[559]

As for the longer strands of isolated DNA, Judge Moore still holds it as a patentable subject matter.[560] The long sequence is unlike the short sequence that can be used for primers as a detection use.[561] The isolated long length gene does not clearly have a new utility.[562] Moreover, she emphasized that if this case can be decided on a blank canvas, she might conclude the long isolated DNA sequence as non-patentable subject matter but today, this is not the case.[563] For past decades, United States Patent Office has granted DNA sequence patents for decades and there is no indication from Congress that this view is wrong.[564] Therefore, holding "the isolated DNA not patentable would destroy long settled industry expectations for no reason other than a gut feeling that DNA is too close to nature to be patentable."[565] Judge Moore thinks the scope of the law of nature exception was certainly enlarged in *Prometheus.*[566]

### 4.6.5 Comparison of Judge Bryson's Opinion

In the previous case, Judge Bryson used an analogy that extracting a gene is like snapping a leaf from a tree.[567] In the new verdict, he also used the example of a human kidney to emphasize his view.[568] He explained "a human kidney is a product of nature; it does not become patentable invention when it is removed from the body, even if the patentee has developed an improved procedure for extracting the kidney and even if the improved procedure results in some physical or chemical changes to the kidney."[569]

Judge Bryson's perspective on Supreme Court decision in *Mayo v. Prometheus* is that case does not decide this case but the Court's analysis is nonetheless

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[559] Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).
[560] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 27 (Fed. Cir. 2012).
[561] *Id.* at 33.
[562] *Id.*
[563] *Id.*
[564] *Id.* at 37.
[565] *Id.*
[566] *Id.* at 33.
[567] *Id.* at 42.
[568] *Id.*
[569] *Id.*

instructive.[570] The method claims in *Mayo* involved the steps of administering a drug to a subject, determining a metabolite concentration in the subject's blood and determine if there is a need for adjustment in dosage based on certain metabolite concentration.[571] The Court found the method claim as non patentable subject matter because it contributed nothing "inventive" to the law of nature that lay at the heart of the claimed invention.[572] The Court focused on whether the claims do "significantly more" than simply describe the natural relations" and whether the "claims add enough to their statements of the correlations to allow the process they described to qualify as patent-eligible processes that apply natural laws."[573] The decision was based on the rationale that the claims did not add "enough" to the natural laws because the processes involve well- understood , routine, conventional activity previously engaged by researchers.[574] A patent involving a law of nature must have an "inventive concept" that does "significantly" more than simply describe.[575] In Judge Bryson's view, the composition claims in this case does not fulfill this requirement. Neither the isolation of naturally occurring material nor the breaking of covalent bonds makes the claimed molecules patentable. The structural changes to the isolated gene do not make these claims patentable because the cleaving of chemical bonds is "not inventive".[576] Also, the fact that cleaved molecules with different terminal groups does "nothing to add any inventive character" to the claimed molecules.[577] The function of the molecule remains identical to the naturally occurring gene.[578]

# Chapter 5 – Assessing the CAFC's Decisions in the *Myriad* Case

## 5.1 – Assessment of Judge's Opinions as Delivered in the *Myriad* Case

### 5.1.1 Issues Solved: Test Method Claims in Gene Patents

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[570] *Id.* at 43.
[571] Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289, 1295 (2012).
[572] *Id.*
[573] *Id.* at 1297.
[574] *Id.*
[575] *Id.*
[576] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 44 (Fed. Cir. 2012).
[577] *Id.*
[578] *Id.*

Before the *Myriad* case, granting the method patent has been a debatable issue. Since the *State Street Bank & Trust Co. v. Signature Financial Group*[579] case until the recent *Bilski*[580] case, different courts hold various views and standards regarding this issue. This intense development over past decades has lead to the result of well established standards. In this new remanded *Myriad* case[581], the method claims for gene sequence seems to follow these established standards. All three judges at the Federal Court have reached the same conclusions that the method patent that involves comparing or analyzing isolated DNA sequences is not patentable.[582] Whereas the method patent for screening potential cancer therapeutics via change in cell growth rates is a patentable subject matter.[583] In the concurring opinion offered by Judge Moore and concur in part and dissent in part opinion offered by Judge Bryson, both did not offer any opinion regarding this issue. This allows the public to infer their "matching" decision making standards and judgment.

Starting from *Benson*,[584] phenomena of nature….mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work."[585] These three exceptions to patent protection are well accepted by USPTO and the courts in U.S. because by granting patents to these exceptions are not the inventions that patent system was enacted to protect. In *Flook*[586], the Court emphasized that "even though phenomenon of nature or mathematical formula may be well-known, inventive application of principle may be patented." This is to say that inventive application of phenomena of nature, mental process, and abstract concepts may all deserve patent protection. In addition, the Court explained "patenting principles cannot be circumvented by attempting to limit the use of the formula to a particular technological environment and to hold would allow a competent draftsman to evade the recognized limitations on the type of subject matter eligible for patent protection."[587] In the final judgment, the Court ruled implementing a mathematical

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[579] State Street Bank & Trust Co. v. Signature Financial Group, 149 F.3d 1368 (Fed. Cir. 1998).
[580] Bilski v. Kappos, 130 S. Ct. 3218 (2010).
[581] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1 (Fed. Cir. 2012).
[582] *Id.*
[583] *Id.*
[584] Gottschalk v. Benson, 409 U.S. 67 (1972).
[585] *Id.*
[586] Parker v. Flook, 437 U.S. 584, 593 (1978).
[587] *Id.*

principle on a physical machine, namely a computer, was not a patentable application of that principle, thus not patentable. In *Diehr*,[588] the Court used the same standards and the Court reached the decision that the overall process was patent eligible because of the way the "additional steps" of the process integrated the equation into the process as a whole. These "additional steps" transformed the process into an "inventive application" of formulas, so patentable.[589]

In *Bilski*, the same standards were utilized and the Court indicated that the machine or transformation test as important clue and not the sole test to determining the patentability of method claims.[590] Until the most recent development on method patent set in *Prometheus v. Mayo*[591], the Supreme Court followed the same standards set in previous mentioned cases. In the rationale, the Supreme Court stated that the claim at issue in this case was weaker than claim in *Diehr* and no stronger than the claim in *Flook* and examining the patents at issue with machine or transformation test; indicating a clear showing of a congruent view in terms of standards used in determining the patentability of method claims.[592]

### 5.1.2 Unsolved Issues: Composition Claims in Gene Patents

In this new *Myriad* case, three judges have dissimilar views regarding the composition of matter claims.[593] There are two different types of composition of matter claims at issue: cDNAs and isolated DNAs that are identical to its natural form except the gene is excised from their natural environment and have truncations on each side.[594] There is no difference in judgment on the issue of granting composition patents for cDNAs because they are non-existent in the natural environment and can be used as probes and primers.[595] However, the major difference lies on the second type of isolated DNA sequence. The ruling was based on the isolated DNA sequences have a distinctive chemical form and also they have been chemically cleaved from their native chemical combination. The Federal Court held the isolated DNAs with a

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588 Diamond v. Diehr, 450 U.S. 175, 191-92 (1981).
589 *Id.*
590 Bilski v. Kappos, 130 S.Ct. 3218, 3230 (2010).
591 Mayo v. Prometheus, 132 S.Ct. 1289, 1292 (2012).
592 *Id.*
593 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1 (Fed. Cir. 2012).
594 *Id.*
595 *Id.*

markedly different chemical structure and declared that it is the distinctive nature of DNA molecules.[596] It is the isolated composition of matter that determines their patent eligibility rather than their physiological use or benefits because many different materials may have the same function.[597] It is emphasized that the genes are best described in patents by their structure and not their use.[598] Also, "the patent eligibility of isolated DNA is not negated because it has similar informational properties to a different, more complex natural material."[599]

In Judge Moore's opinion, she first divided the isolated gene sequence into two categories: short sequence and long sequence.[600] She explained the short DNA sequences not only have new and distinct in form, but also new utility such as it can be used as primers or probes in a diagnostic screening process.[601] Natural DNAs do not have the requisite chemical and physical properties needed to perform these functions. The ability to use isolated DNA for diagnostic test is clearly an "enlargement of the range of…utility" as compared to nature.[602] Thus it is not the chemical change alone that lead to the conclusion of the short isolated DNA sequence as patentable subject matter. The different and beneficial utility must also be considered.

As for the long isolated sequence, in Judge Moore's opinion, it cannot be used as primers or probes like the short sequence.[603] Therefore, Judge Moore indicated if she can decide this case on a blank canvas, she might conclude that long isolated sequence as non-patentable subject matter.[604] But she rely her decision on the settled expectation by USPTO on granting the gene patents.[605] She believes "leaving intact the settled expectations of property owners is particular important in light of the large number of property rights involved, both to isolated DNA and to purified natural products generally"[606] and "courts must be cautious before adopting changes that

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596 *Id.* at 19.
597 *Id.*
598 *Id.*
599 *Id.*
600 *Id.* at 28.
601 *Id.* at 30.
602 Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).
603 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 33 (Fed. Cir. 2012).
604 *Id.* at 33.
605 *Id.*
606 *Id.* at 34.

disrupt the settled expectations of the inventing community."[607]

Even though Judge Moore's decisions are not only based on the "chemical distinctiveness" set by the majority opinion.[608] She also focused on the utility of genes. But overall, she still agrees to grant the composition claims. Utility requirement is set forth in 35 U.S.C §101 and the Utility Examination Guideline 2001 published by USPTO affirms the requirement of utility when granting patents.

Judge Bryson delivered a completely different opinion. His view disparages from other judges because he thinks the granting patents to isolated sequence is granting the genes themselves which appear in nature on the chromosome of living human beings.[609] The only material change to those genes is "the changes that is necessarily incidental to the extraction of the genes from the environment in which they are found in nature."[610] The isolated genes are not materially different from the native genes. He then focused on the majority opinion regarding the isolated genes are new molecules and cleaving those bonds to isolate BRCA genes turns them into patentable subject matter.[611] Judge Bryson explained there is no magic in breaking a bond, the gene remains to be the same whether the gene is in the body or isolated.[612] Also, he pointed out that claim 1 of '282 patent included gaps denoted "vvvvvvvvvvvv" and this could result with an incalculable large number of molecules that would fall into the scope of this claim.[613] The composition claims have the same sequences as their natural form, they code for the same proteins and they represent the same units of heredity. Also in '282 claim 6 covers any sequence of the BRCA1 cDNA that is at least 15 nucleotides long.[614] This short sequence claim has given a broad protection because it is very likely to be included in other portion of genes.[615] This then raises the concern for the future development of multiplex test and whole genome sequencing.

This is a clear showing of disparage views on granting composition of matter

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[607] Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 739 (2002).
[608] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 32 (Fed. Cir. 2012).
[609] *Id.* at 39.
[610] *Id.*
[611] *Id.*
[612] *Id.*
[613] *Id.* at 41.
[614] *Id.* at 45.
[615] *Id.*

patents in the Federal Court. The standards used were also different as well. Majority supports the determination solely on the distinctive chemical characteristics.[616] Judge Moore suggests evaluating patentable subject matter by using both the distinctive character and utility.[617] Whereas, Judge Bryson negates the patentability of composition of matter for genes because they are identical to the natural form and by granting patents may have number of negative effects.[618] The overall standards used in the majority opinion are the least restrictive in granting gene patents. This shows the past standard in granting gene patents. However, since the prevalent patents granted to ESTs in early 1990s where many of their functions were still not identified.[619] This resulted the over protection of the ESTs and this is one major reason why the Utility guideline was set to prevent a similar problem.[620] In this case, majority made the final judgment only based on the chemical distinctiveness of the gene. This can rather be insufficient because manipulations of gene sequences by altering some unimportant or unneeded can be easily achieved in the field of technology. Judge Moore suggested a more restrictive method of granting gene patents.[621] But overall, Judge Moore showed similar attitude of providing patent protection for composition claims. She recommended granting patents for short sequence based on it can be used for primer and probes.[622] The benefits of utility make granting the composition more just. However, Judge Bryson's view that short gene sequence has broad protection is correct.[623] The short gene sequence is very likely to appear somewhere in some other long gene sequence.[624] This may eventually result with blocking and stifling effect on the future research.[625]

By denying granting of composition patents for genes may overthrow past thirty years in granting gene patents. This may result incalculable effect to biotechnology industry due to the impact of invalidating the previous granted patents and also affect

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[616] *Id.* at 33.
[617] *Id.*
[618] *Id.* at 39.
[619] Tom Reynolds, *Pricing Human Genes: The Patent Rush Pushes On,* JOURNAL OF NATIONAL CANCER INSTITUTE 92, 96-97 (2000).
[620] *Id.*
[621] Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 27 (Fed. Cir. 2012).
[622] *Id.* at 31.
[623] *Id.* at 45.
[624] *Id.*
[625] *Id.*

the industry's incentive to invest in future research.

### 5.1.3 Do the Decisions in the *Myriad* Case Derailed from the Precedent Cases and the Statute?

Federal Court Judges in the *Myriad* case have showed similar perspective in regarding granting method patents.[626] The physical phenomena, law of nature and abstract ideas are first evaluated because these are exceptions to patent protection.[627] The first type of method claims that involved comparing and analyzing sequences was held non-patentable because the Court ruled it is simply an abstract mental process to compare two sequences.[628] The comparison was merely an inspection. Therefore, the claims are not patentable.[629]

The second type of method patent involves screening potential cancer therapeutics. Again, the Court first reached the claims are not natural product. The Court then emphasized "to transform an unpatentable law of nature into a patent eligible application of such a law, one must 'do more' than simply state the law of nature while adding the words 'apply it'."[630] The decision was reached under the evaluation of machine or transformation test.[631]

Regarding the composition of matter claims, three Federal Court judges in the Myriad case share same perspective as to the patentability of cDNAs.[632] The ruling was based on the non existence in the natural environment, difference in structure and function as probes. However, the patentability of composition claims was never a central issue in any of the previous cases. Thus, the standards are not as well established compare to method claims. Nonetheless, the dissimilar views in granting the composition of matter patents for isolated gene sequence authenticated this fact. Judge Bryson has placed the consideration of the overbroad patent scope in blocking

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626 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 31 (Fed. Cir. 2012).
627 *Id.* at 17.
628 *Id.* at 25.
629 *Id.*
630 Mayo v. Prometheus, 132 S.Ct. 1289, 1294 (2012).
631 *Id.*
632 *Id.*

future research as one reason in repudiating grant of gene patents.[633] With the drastic increase importance in genetic testing, patent protection may play a part in the future biotechnology development.

Article I, Section 8, Clause 8 of the United States Constitution set to promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries. On the issue of method claims, the decisions of the Federal Court are showing stricter rules in determining the patentability of method claims. The three exceptions to patentability, application of those exceptions, and the machine or transformation test are all the required tools.

On the issue of composition claims, the decision from each judge is different. From author's point of view, Judge Moore and Judge Bryson's opinions are more analogous to the elements set in the statute.[634] In the new remanded *Myriad* case, the determination of utility in evaluating patentable subject matter was not a requirement.[635] From the statute, clearly "usefulness" of the invention must take into account in determining the patentability of inventions. Judge Bryson focused his rationale mainly on the nature of the gene sequence, stating it is the same as the natural form and in considering the overbroad protection of patent scope may eventually stifle and not promote the progress of science.[636] In addition, Judge Bryson did also consider the utility of the claims by focusing the probe and primer use function.[637]

## 5.2 – How Do the Decisions of CAFC in This Case Affect the Research Access, Patient Access and Incentives to Invest?

Until now, there is no particular trend in the type of patent that Federal Court is likely to grant in terms of gene sequence. However, there is a tendency of more strict

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633 Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 38 (Fed. Cir. 2012).
634 *Id.*
635 *Id.*
636 *Id.* at 37-39.
637 *Id.*

and well set standards for method claims. The Federal Court is showing granting more protection to composition claims with less strict evaluation standards. Both composition claims at issue were ruled to be valid. This lead to the concern of the effect by giving more protection to composition claims.

One disadvantage of granting composition claims is this type of patent allows the protection to extend to all subsequently invented new uses and even if they were not anticipated in the patent application.[638]The unique character of gene study is that genes have unknown functions, some produce several proteins and play different roles in gene expression.[639] Many functions are still need to be identified. Thus, this is one reason why many groups support the opposition of granting composition patents such as Nuffield Council.[640] Also, several technologies have been developed for simultaneously testing multiple genetic markers with one single test.[641] Compare this with the past technology, each genetic marker would be tested in a separate test. Therefore, this makes the testing complex, time consuming and expensive. In comparison, multiplex testing would be more efficient and potentially less costly.[642] One potential problem of granting many composition patents is the higher probability to infringe the claims in one multiplex gene sequencing.[643] Especially there is high tendency of developing this technology in modern and future world.[644] Thus, this may increase the necessity for negotiations in licensing of those genes.

One common multiplex testing the gene microarray, it is consist of substrate of specific nucleic acid molecules or genetic molecules that may react with or "hybridize" with complementary DNA fragment molecules.[645] The problem of granting composition patents is that the probe molecules or the molecules that are attached to detect or react with desired sequences, may infringe any claims to identical or equivalent gene sequence molecules useful as probes.[646] The number of licenses

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[638] Sirp Soini et al., *Patenting and licensing in genetic testing: ethical, legal and social issues*, EUROPEAN JOURNAL OF HUMAN GENETICS 16, S10-50 (2008).
[639] *Id.*
[640] *Id.*
[641] SACGHS report, *supra* note 133, at 29.
[642] *Id.*
[643] *Id.*
[644] *Id.*
[645] *Id.*
[646] Patent 5,622,829 contains claims to such fragments.

required of developing the microarray technology depends on the how many genes are protected by patents. So far, according the reference shows 20 % of the genes that are identified are under protection of patents.[647] This may show a potential for patent thick problem in the future and most importantly, this may discourage the researchers the desire to pursue the development of the multiplex tests.

As for granting method patents, Federal Court has more well developed standards compared to the composition patents. The previous study shows that method patent in the gene sequence circumstances is difficult or impossible to circumvent. The reasons include method of genetic diagnosis not specified by claim language and the broad wordings are used.[648] With more clear standards in evaluating the gene sequence method patents, this can provide more clear lines for the researchers and the public to understand how can gene patents be granted. But, after the patentability of gene sequence in granting method patent is confirmed, then the scope of the claim must also be examined in later phases prior to granting patents in order to prevent the over broad protection of method claims because the difficulty in or impossibility to circumvent the patent scope of the method claim may also result with patent thicket problem. Therefore, if the method patents are continued to be granted by USPTO, then the examination for overbroad patent scope is need it.

Permitting the gene sequences patents is correlated to the patient access. With high probability of impossible and difficult to circumvent the method claims, it is likely to require license fees. The license fees will eventually transfer to the future patient users. Not only license fees but also shipping fees when there is only one sole provider and the research fee associated with the searching of existing gene patents and progress of patent application. The future development of multiplex gene tests and whole genome sequencing tests will require multiple license fees for each of the composition claims. This can also lead to increase in cost for patients. Aside from increase in cost, future patients will have less access to second opinions as the patentee is the only sole provider of such diagnostic test.

On the other hand, providing less patent protection or no patent protection may affect the incentives to invest and disclose the relevant technologies. This excludes the

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[647] *Id.*

[648] Isabelle Huys et al., *Legal uncertainty in the area of genetic diagnostic testing*, 27 NATURE BIOTECHNOLOGY 903, 907 (2009).

researchers who pursue genetic study because of academic reasons or personal reasons such as pure curiosity. Except for those companies or some researchers that do consider patent as one of their primary motives. By providing less or no patent protection may slow down the speed of future invention developments due to less incentive to disclose the relevant technologies. People may prefer to keep the technologies as trade secrets, thus, slow down or unable to develop new inventions due to insufficient disclosed technologies.

The Vice President for Research and Technology Management at Case Western Reserve University stated that a genetic test aimed at detecting early stage colon cancer is being commercially pursued because the university was able to exclusively license the associated patent rights.[649] Also, Director of Licensing at the University of Michigan has indicated the same situation in the five gene panel test for lupus erythematosis.[650] The Director explained patents will motivate the licensee to "invest in both further university research as well as in clinical trials to validate the use of the DNA panel."[651] Axial Biotech and Juneau Biosciences both also agreed that patents influenced outside investors.[652] Thus, protecting their genetic tests through the patent system has been "a major fact" in persuading some investors that their products will make profit.[653]

The dilemma between granting patent protection for gene sequence involves research access, patient access and the one of the primary motives of patent system, provide incentives for potential developers. From author's point of view, it is very unlikely the USPTO and U.S. courts to invalidate all gene patents granted over past thirty years or stop granting gene patents because this may have an incalculable impact in the field of biotechnology and bio-pharmacology. Nonetheless, with difficulty to circumvent the method claims must take into consideration because in the long run it may also affect the development of multiplex gene tests similar to the effect of granting the composition claims.

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649 SACGHS report, *supra* note 133, at 29.
650 *Id.*
651 *Id.*
652 *Id.*
653 *Id.*

# Chapter 6 – The Possible Solutions to Gene Patenting

Aside the understanding of the Federal Court's most recent view on the issue of whether human gene can be treated as a patentable subject matter, further consideration of how to solve the negative impact caused gene patents such as causing a delay or obstacle in research or patient access would also be pivotal. Since the first patenting of gene sequence until now, decades of precedent cases, it is doubtful the Court will refer back to their previous decisions and ban all the gene patents. Hence, without this extreme possibility, what are some solution possibilities to granted gene patents? Also, what are some measures that can be used by USPTO in terms of the granting gene patents in the future?

## 6.1- Alternatives in solutions

### 6.1.1 Compulsory Licensing

One of the options that may balance the competing interest of encouraging companies to continue pursuing the long and expensive research is the compulsory licensing. This is a common policy among EU Member states and TRIPs members as many of them have provisions in their laws for compulsory licensing. The Doha Declaration tried to solve the problems regarding the availability of pharmaceutical products in the developing countries by allowing the member states to have more flexibility to integrate social policy goals.[654] Nonetheless, this policy is build on the condition that it must be compliant with the TRIPs Agreement.[655]

Compulsory licensing regulation was set under WTO TRIPS art.31.[656] This enables the government in developing and least developed countries to use the patented invention without the permission of the patent holder in order to allow another manufacturer to produce this medicine in certain stipulated circumstances.[657] Furthermore, art 31(a) articulated that compulsory license can only be granted under

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654 *Id.*

655 *Id.*

656 Andrew W. Torrance, *Patents to the Rescue--Disasters and Patent Law*, 10 DEPAUL J. HEALTH CARE L. 309, 336-40 (2007) (noting that the United States has rarely used compulsory licensing, primarily in the context of air pollution control and nuclear energy).

657 TRIPS Agreement, at http://www.wto.org/english/tratop_3/trips_e/t_agm0_e.htm (last visited March 14, 2012).

limited circumstances and it functions on a "case-by-case" basis.[658] The circumstances like "national emergency" or "extreme urgency" and limitation of "public non-commercial use.[659]" The scope and duration of use under the compulsory license is limited to "the purpose for which it was authorized" which is set by art.31(c).[660] In U.S., the similar "march-in right" maintained under the Bayh-Doyle Act allowed the government to "march-in" the commercialization and public availability on federally funded inventions.[661]

Overall, the enforcement of compulsory licensing may lie in the hands of national laws and court practice.[662] Nonetheless, there is a possibility of delay caused by domestic legislation. Also, many bilateral and regional free trade agreements restrict the use of compulsory licensing as well.[663] Particularly for U.S., has increasingly included intellectual property chapters in their bilateral and regional FTAs.[664] The intellectual property chapters often include "TRIPS-plus provisions" and these provisions often limit or prevent the use of TRIPS flexibilities such as compulsory licensing.[665]

Even though compulsory licensing can provide a speedy solution to gene patent problem, but this is may not be the ultimate solution for gene patenting because it may involve various factors such as domestic legislation and TRIPS-plus provisions in FTAs. Ultimately, this may affect the inventors' right to commerce and reduce incentive to invent.

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### 6.1.2 Research Exception

The concept of the fair use exception first originates in copyright law and it has

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[658] TRIPS art.31 (a): "authorization of such use shall be considered on its individual merits" and the legal validity of each compulsory license is subject to independent review.

[659] F.M. Scherer & Jayashree Watal, *Post-TRIPS Options for Access to Patented Medicines in Developing Nations*, JOURNAL OF INTERNATIONAL ECONOMIC LAW 913, 914 (2002).

[660] TRIPS art. 31 (c).

[661] Miri Yoon, *Gene Patenting Debate: The Meaning of Myriad*, 9 J. MARSHALL REV. INTELL. PROP. L. 953, 969 (2010).

[662] *Id*.

[663] Jenny Wakely, *The impact of external factors on the effectiveness of compulsory licensing as a means of increasing access to medicines in developing countries*, E.I.P.R. 756, 770 (2011).

[664] Collins Chase, *The case against TRIPS-Plus Protection in Developing Countries Facing AIDS Epidemics*, UNIVERSITY OF PENNSYLVANIA JOURNAL OF INTERNATIONAL LAW 763, 778 (2007).

[665] *Id*.

been suggested that this concept can be also utilized in patent law to promote an appropriate balance between encouraging innovation and maintaining the progress via public access.[666] The fair use exception permit the use of the patented gene by third parties in the absence of a license without been sued for infringement. The rationale behind the experimental use exemption is to prevent patent stifle the progress of scientific progress by slowing the research. The overbroad exclusion protection may decrease the efficiency of patented gene.[667] Hence, the exception to limit the patentee's patent protection may avoid potential development of an anti-common for genes.[668]

One of the SACHGS's proposed solutions for gene patent is the creation of an exemption from patent infringement liability for those who use patent protected genes in the pursuit of research.[669] Moreover, further differentiate between commercial and noncommercial research. But, it has been suggested the research exemption should focus only on noncommercial research[670] and most importantly, not adversely affecting the returns for the patentee's investment.[671] Nagaoka and Aoki showed that research exemption is particularly beneficial when the nature of the final product is unknown.[672] Nonetheless, the nature of the product may depend on whether it is commercial product or not.[673] This solution may benefit because it allows "the research and development to make testing more comprehensive, more accurate or less expensive," therefore improving the testing quality.[674] It has been suggested that research exemption will allow the downstream research to perform the experiments without a license and this has been proven to be effective when inventing around the gene patent is difficult.[675] Also, there are suggestions that support the making research exemption mandatory for those who receive public funding like NIH's policy

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666 Marueen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law,* 100 COLUM. L. REV. 1177 (2000).
667 *Id.*
668 *Id.*
669 SACGHS report, *supra* note 133, at 87.
670 Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use,* 56 U. CHI. L. REV. 1017, 1034-35 (1989).
671 Soini et al,, *supra* note 638, at S10-50.
672 *Id.*
673 *Id.*
674 Robert Cook-Deegan et al., *The Dangers of Diagnostic Monopolies,* 485 NATURE 405, 406 (2009).
675 *Id.*

in U.S.[676]

In TRIPS Agreement, it listed that "members may provide limited exceptions to the exclusive rights conferred by patents as long as it does not unreasonably conflict with "the interest of the patent holder."[677] Although, this provision may not be clear but based on the legislative history, it is likely that this article is enacted to allow exceptions for private, noncommercial purposes, research, experimentation for testing or improvement and educational purposes.[678]

Even though there is no identical exception in current U.S law. But there is a limitation on patent infringement for medical procedures, added in 1999 at 35 U.S.C. § 287: (c)(1) With respect to a medical practitioner's performance of a medical activity that constitutes an infringement . . ., the [infringement] provisions . . . of this title shall not apply against the medical practitioner or against a related health care entity with respect to such medical activity. (2) For the purposes of this subsection: (A) the term "medical activity" means the performance of a medical or surgical procedure on a body, but shall not include (i) the use of a patented machine, manufacture, or composition of matter in violation of such patent, (ii) the practice of a patented use of a composition of matter in violation of such patent, or (iii) the practice of a process in violation of a biotechnology patent.[679] This provision clearly limits the protection of medical practitioners who infringe a patent in the course of medical or surgical procedure. Thus practitioners of diagnostic testing are excluded from liability exemption. Therefore, it has been suggested to congress that the 35 U.S.C. § 287(c) needs to be broadened to include the use of practitioners who perform diagnostic tests.

However, before setting up the fair use exception, it first must be evaluated with caution. Professor Maureen O'Rourke has provided a five factor framework for a fair use analysis.[680] The first factor is "the nature of the advance represented by the infringing work."[681] The second factor "the purpose of the infringing work"[682] The

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[676] *Id.*

[677] The American Society of International Law, General Agreement on Tariffs and Trade-Multilateral Trade Negotiations: Agreement on Trade Related Aspects of Intellectual Property Rights, Including Trade in Counterfeit Goods, in International Legal Materials.

[678] Carlos M. Correa and Abdulquawi A. Yusuf eds., Intellectual Property and International Trade: The TRIPS Agreement, London: Kluwer Law International 189, 208 (1998).

[679] 35 U.S.C. § 287 (2006).

[680] O'Rourke, *supra* note 666, at 1205-09.

[681] *Id.* at 1206.

third factor is "the nature and strength of the market failure that frustrates licensing."[683] The fourth factor is "the impact of the use on incentives and social welfare."[684] The fifth factor is "the nature of the patented work."[685] After careful scrutiny of these factors, fair use could potentially solve the problem of gene patents in stifling the research.

### 6.1.3 Granting of the "Function-specific" Patent

The patentable subject matter and scope of patent protection are two different issues. However, these two issues are related as they may follow in a sequential relationship. Patentable subject matter must be determined prior to the scope of protection. If the invention does not qualify the patentable subject matter then patent would not be granted and thus no need to determine the scope. However, now understand the Federal Court's most view human gene sequence as patentable subject matter, the issue of patent protection scope then play a significant role. The scope of composition patent and process patent are different because the composition patent scope includes the product itself and the process of making it. Allowing composition of matter claims will enable the patentee to control the future applications of the patented gene sequence.[686] As the biotechnology shift toward new classes of diagnostic that involve simultaneously detecting multi-genes or entire genome, the importance of granting composition of matter patents ascends. The complex intellectual property landscape of DNA patents may involve challenges for future multi-genomic, parallel sequencing or full genome diagnostics.[687] With closer relationship between genes and patent protection, the potential of blocking or patent thicket problem may begin to rise. Therefore, granting more composition of matter patents that can result a broader scope compare to process patent in general may not be an appropriate development for gene patents.

Even though the scope of the method or process patent only protect the process

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[682] *Id.*
[683] *Id.*
[684] *Id.*
[685] *Id.*
[686] Subhashini Chandrasekharan and Robert Cook-Deegan, *Genome Medicine Gene patents and personalized medicine – what lies ahead?* GENOME MEDICINE 1:92 (2009).
[687] *Id.*

and not the end product thus provide lesser protection when compare with the composition of matter patent. But the research data shows method claims are difficult to circumvent in terms of performing the future diagnostic test.[688] The reason being the exact method of genetic diagnosis is not specified by the claim language and broad wordings are used.[689] The blocking gene patents claims identified are formulated broadly in covering many types of genes.[690] Diagnostic method claims generally confer protection for a series of working steps and if the claim broadly formulates the link between mutation and disease without specifying steps as how this link is determined, so, it is unclear the scope of the patent.[691] For example, US 5693470 and EP1015628 are both method claims that are almost impossible to circumvent.[692] In these patents, the claim refers to the use of "any" test and this claim is so broad that it can cover an indefinite number of tests.

In the same study, the researchers have identified that nearly half of 145 patents and 267 independent patent claims are classified into four categories.[693] The four categories include methods, gene, oligo, and kits.[694] The percentile of each is 38%, 25%, 23% and 14% respectively.[695] The claims that are difficult to circumvent or impossible to circumvent are mainly method claims.[696] Among all the method claims, 30% is measured as impossible to circumvent and 47% is measured as difficult to circumvent.[697] This data showed the granted method claims are a greater concern.

In continuing granting the gene patents by USPTO, the potential harmful future effect of granting composition patents or method patents should be carefully considered. If a patent can be granted only for the specified use or application of the gene sequence that limit the protection scope, this may prevent the stifle effect of future research, especially in the field of multi-gene diagnostic development and full genome development. Granting function-specific patent may reduce the overall

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688 Isabelle Huys et al., *supra* note 648, at 903–05.
689 *Id.*
690 *Id.*
691 *Id.*
692 *Id.*
693 *Id.*
694 *Id.*
695 *Id.*
696 *Id.*
697 *Id.*

incentive generated by the patent, but in the long run, the biotechnology or pharmaceutical company may worry less about invalidation of their patents because of more specific and smaller scope. This theory can be supported by the increase importance in diagnostic test in the near future, may most likely lead to a greater competitive development of this field's technology and as a result, more people may challenge the validity of the patent.

### 6.1.4 Patent Pool

A patent pool is an agreement between two or more patent owners to license one or more of their patents to one another or third parties."[698] All the patent holders within the patent pool agree on reasonable licensing and royalty fees when members use the protected inventions.[699] Patent pool can provide the means necessary to disseminate information quickly to facilitate further research while eliminate licensing costs.[700]

Patent pools are usually organized by independent organizations that can also negotiate licensing with non-member researchers who wants to use the information within the pool. It has been suggested the criteria for setting for a patent pool should include: voluntary in nature, incentives for voluntary participation, restricted access to the patent pool, and selection of proper management team such as a reputable international organization such as UNITAID.[701]

One major concern of setting up a patent pool is be able to convince the innovators how combining the patents can bring them benefits such as producing a superior product. The possible benefits are as follows. First, the chances of refusing to license the patented inventions by patent holders will be greatly reduced. Therefore, vital genetic information can be utilized to develop tests and products.[702] Second,

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[698] James Bradshaw, Comment, *Gene Patent Policy: Does Issuing Gene Patents Accord With the Purposes of the U.S. Patent System?* 37 WILLAMETTE L. REV. 637, 645 (2001).

[699] Shanshan Zhang, *Proposing Resolutions to the Insufficient Gene Patent System*, 20 SANTA CLARA COMPUTER & HIGH TECH L.J. 1139, 1167-8 (2004).

[700] Jeanne Clark et al., U.S. Patent & Trademark Office, *Patent Pools: A Solution to the Problem of Access in Biotechnology Patents*? (2000), available at http://www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf.

[701] Eric Noehrenberg, *Implications of Patent Pools on Innovation Regarding Antiretrovirals*, THE OPEN AIDS JOURNAL. 4, 69 (2010).

[702] Jeanne Clark et al., Clark, *supra* note 700, at 8.

patent pools can avoid the cost associated with multiple licenses such as when one complete sequence is held by many different patent holders.[703] By having a patent pool allows interested user to deal with only one administrator and pay only one fee.[704] Also, avoidance of having to pay a increased royalty when the patent holder understands his/her invention (a genetic sequence) is the last patent that is required before the interested user conducts his/her research. Third, DNA samples can be send to more than one laboratory whereas comparing sending the sample just to the exclusive patent holder, so providing confirmation can be done at a lower fee.[705] Forth, the risk can be allocated to different members in pool when each member receives a certain percentage of total royalties collected thus aid to research and development expenditures.[706] These potential benefits may help to resolve the gene patent problem, but whether or not it is the ultimate solution remain to be evaluated.

The formation of patent pool can be time consuming because it involves first setting proper criteria for the patent pool, multi licensing processes, and accumulation of large number of patents. But, this policy in the long term can possibly bring many benefits. Especially for biotechnology corporations, this policy can provide a financial insurance that may increase the likelihood that the company will recover the research and development costs.[707]

## Chapter 7 – Conclusions

With advance in biotechnology, prolonging the life of human beings and enhancing better medical treatments are becoming more important. This fact can be supported by the drastic increase of patent application and granted patents in U.S. As gene diagnostics become more prevalent, the issue of patentability of these genes becomes a vital issue. *Myriad* case is such critical case because the decisions in this case may dictate the future development in diagnostic test. Patentability of genes does not only influence the diagnostic field, but also drug related field as well. From

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[703] Zhang, *supra* note 699, at 1169; Clark, *supra* note 700, at 8.
[704] *Id.*
[705] *Id.*
[706] *Id.*
[707] Steven C. Carlson, *Patent Pools and the Antitrust Dilemma*, 16 YALE J. ON REG. 359, 381-82 (1999).

analyzing the *Myriad* case and in comparison with the precedents, a conclusion can be reached. The gene method claims are evaluated with more clear and established standards due to more complete development. Whereas, the composition claims are evaluated with different standards and therefore different decisions were reached.

The role of Patent is to promote the progress with science and discoveries by providing an incentive to patent applicants. Unlike other technologies, with definite know function, the exact function of each gene is difficult to find. Thus, by granting patent protection to these genes may ultimately stifle the future research and not to promote science. Hence, this is a rather complicated issue to solve as this issue may involve various fields of people, study and industry.

In author's view, it is very unlikely the USPTO and courts will invalidate all gene patents or stop granting gene patents. Although, 67% of genetic related researches performed in U.S. are government or public funded[708], leaving nearly 33% is privately funded companies that may rely on the patent protection as a necessary incentive to invest and continue research. For example, take into consideration of the patentee of the case, Myriad Genetics, the BRCA tests alone account up to 86.4% of the company revenue in 2011.[709] Thus, leading to an inference that patent protection may play a significant role in a biotech company. Invalidating gene patents or stop granting gene patents may have an incalculable effect that is more detrimental than stifling the future research. Without the existence of new inventions, patients may be more serious affected in the long run. This is not to deny a vast amount of inventions are result from public or government funded projects. Therefore, some alternate solutions are required to make up the problems caused by granting gene patents. Different solution can be utilized depending on the immediacy of the circumstance as some solutions may require longer time to enact.

Overall, gene patent should still be granted in providing an incentive like the original purpose of setting patent protection in the U.S. Constitution. However, more clear standards should be established in evaluating the patentability of the gene sequence. The special circumstances in gene patents of unknown function and the

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[708] Ass'n of Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 210 (S.D.N.Y. 2010).
[709] Peter D. Meldrum, *supra* note 367, at 3.

need of multiplex diagnostic development, should also be taking into consideration. The *Myriad* case has already opened the door for the public to focus on the validity of gene sequence. Since this issue already has become an inevitable problem, it would be better to solve it now as it would be more difficult to solve as time elongates due to the immeasurable potential impact.

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