Patentability and Biotechnology Innovation: Decoding the Current Legal Framework for Patent Eligibility of Natural Phenomena-Based Biotechnologies

I. Defining the Problem: Do the Current Patent Laws Strike a Just Balance?

At the heart of this study lies a fundamental question: does American patent jurisprudence properly stimulate biotechnology innovation, while maintaining true 'products of nature' as outside the realm of patentability, or has this body of legal precedents erroneously expanded the 'product of nature' exception in such a way that biotechnology innovation is now impeded by the very system intended to foster its growth?

This query is more than just an intellectual curiosity. Rather, the breadth of patent protection for biotechnological products and methods of treatment has pervasive effects on the nature of scientific research undertaken into these arenas, as well as the development of new diagnostic and therapeutic products. Certainly private companies looking to make money from the research and development of biotechnology products will look to the patentability of potential products in projecting potential profitability against commercialization costs, because patents confer exclusivity rights to those patent holders. However, even if post-development profitability is not a principal concern for a biotechnology firm, patentability remains a critical determinant of what research and development is undertaken because large numbers of firms must rely on venture capital investment to fund their research, testing and product development, and those investors will look to the intellectual property portfolios and the value of patents in those portfolios in determining whether to invest (Johnson 2017). Thus, patentability

jurisprudence not only influences, but actually dictates, the nature of biotechnology research and the therapies that ultimately become available to patients.

II. Enactment and Interpretation of Patent Laws

The United States Constitution gives Congress the power to "promote the [p]rogress of...useful arts by securing for limited [t]imes to…[i]nventors the exclusive…[r]ight to their…[d]iscoveries." (U.S. Const. art. I, § 8, cl. 8). With such authority, Congress established the U.S. Patent and Trademark Office (hereinafter "USPTO"), which has the responsibility for issuing patents and trademarks according to the laws enacted by Congress (35 U.S.C. §§1, 2). A U.S. patent gives its owner "the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States" (35 U.S.C. §154(a)). Congress codified patentable subject matter as "…any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" (35 U.S.C. § 101).

The U.S. federal courts have exclusive jurisdiction over causes of action "relating to patents" (28 U.S.C. § 1338(a)) and the decisions of these courts constitute the interpretations and applications of these patent laws. The Court of Appeals for the Federal Circuit (hereinafter "the Federal Circuit") has exclusive jurisdiction over all appeals in patent actions (28 U.S.C. § 1295), rendering the decisions of this Court particularly meaningful. Some appeals of the Federal Circuit are granted certiorari by the United States Supreme Court, and as it is the highest court in the country, the Supreme Court is the ultimate authority in interpreting and applying the patent laws enacted by Congress.

III. Patent-Eligibility and the Doctrine of Preemption

The U.S. Supreme Court has promulgated three *exceptions* to the broad patent-eligibility principles set forth in 35 U.S.C. § 101: (1) laws of nature, (2) physical phenomena, and (3) abstract ideas (*Diamond v. Chakrabarty*, 1980). Decades after its decision in *Chakrabarty*, the Supreme Court further explained the rationale driving these three specific exclusions to patent eligibility "as one of pre-emption" (*Alice Corp. Pty. v. CLS Bank Int'l*, 2014). Noting that laws of nature, natural phenomena, and abstract ideas are "the basic tools of scientific and technological work," the Supreme Court reasoned that patents of such tools may result in monopolizations thereof that would "tend to impede innovation more than it would tend to promote it" (*Alice Corp. Pty. v. CLS Bank Int'l*, 2014).

Fearing innovation-stifling appropriation, the Supreme Court decreed that patent law must distinguish between those claims to "'building[g] block[s]' of human ingenuity" versus those that "integrate the building blocks into something more, thereby 'transform[ing]' them into a patent-eligible invention" (*Alice Corp. Pty. v. CLS Bank Int'l*, 2014 (quoting *Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012)). Per the Supreme Court, the exclusion of laws of nature, natural phenomena, and abstract ideas from patent-eligibility avoids "disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries" (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). Driving this preemption doctrine is the concern that the holder of a patent on a natural law, natural phenomenon or abstract idea can prevent all further developments in the respective field because the use of that very law, phenomenon or idea is essential to it being improved upon (Tallmadge 2017).

IV. Shifting Boundaries of Patent-Eligibility

Though the doctrine of preemption may be laudable in theory, in practice the Supreme Court has issued a series of decisions which fail to clearly differentiate between patent-ineligible claims to natural laws, natural phenomena, and abstract ideas versus patent-eligible claims that "amount[] to significantly more than a patent upon the [ineligible concept] itself" (*Alice Corp. Pty. v. CLS Bank Int'l*, 2014). Undoubtedly, the Supreme Court's recent decisions of *Prometheus Labs. Inc. v. Mayo Collab. Servs.* (hereinafter "Prometheus") and *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* (hereinafter "Myriad") were attempts to strike a just balance in biotechnology patent law between creating incentives to discovery without resulting in a monopoly that would improperly limit further scientific inquiry into the natural world. Whether one agrees with the outcomes of the decisions or not, most legal scholars, patent practitioners, and scientists agree that these decisions have added uncertainty in the preparation and value of life sciences patents, and this resultant lack of certainty disincentivizes investment and pursuit of many forms of health-related research and innovation (Schaffer, et al. 2019; Carson & Mulvaney 2018; Johnson 2017; Tallmadge 2017; Cloney 2016; Bernstein 2015; Gordon 2015; Hoxha 2015; Lauzon 2014).

Before diving into the *Prometheus* and *Myriad* cases, let us first examine the historical context in which these decisions arose.

A. "Isolated" and "Purified" – Focusing on the Inventive Step to Isolate/Purify and the Therapeutic Purpose Derived Therefrom

It is perhaps unsurprising that problems would arise in the 21st-century application of the preemption doctrine where nearly a century worth of biotechnology patent claims had been approved by the USPTO based upon court interpretations of 'laws of nature' from as long ago as 1911. In *Parke-Davis & Co. v. H.K. Mulford Co*., the famed jurist Learned Hand explained why

purified adrenaline was deserving of patent eligibility, although he conceded that it was possible to conclude that the claimed patent was a product of nature (*Parke-Davis & Co. v. H.K. Mulford Co.*, 1911). The court concluded that the purified adrenaline "became for every practical purpose a new thing commercially and therapeutically" since the inventor "was the first to make it available for any use by removing it from the other gland-tissue in which it was found" (*Parke-Davis & Co. v. H.K. Mulford Co.*, 1911).

Nearly four decades later, the Fourth Circuit Court of Appeals upheld a patent to vitamin B_{12}-active compositions, distinguishing between products of nature and patent-eligible products isolated from nature by focusing on the *purposes* served by the product (*Merck & Co. v. Olin Mathieson Chemical Corp.*, 1958). Similar to the reasoning in *Parke-Davis*, the court in *Merck* reasoned that because the "natural fermentates [forms of vitamin B_{12} existing in nature]…were wholly useless and were not known to contain the desired activity in even the slightest degree[,]" but the purified product was "of great therapeutic and commercial worth," the significance of the medical breakthrough warranted patent rights not only to the process of purification but also to the isolated or purified product itself (Gordon 2015; *Merck & Co. v. Olin Mathieson Chemical Corp.*, 1958; *Parke-Davis & Co. v. H.K. Mulford Co.*, 1911).

Applying these legal tenets, thousands of biotechnology patent claims in the subsequent decades utilized the word "isolated" or "purified" to signify a biological product for which there had been an inventive contribution to its identification and which was delivered in a useful form that had not previously been possible (Gordon 2015). Following this practice, the USPTO awarded patents for product claims to "isolated" DNA molecules which encoded useful proteins (Gordon 2015). Distinguishing such claims from the patent-ineligible 'product-of-nature'

exception, the term “isolated” indicated that the DNA molecule being claimed was distinct from its form in nature, as it had been removed from its natural environs and would not exist in nature in that isolated form (Gordon 2015). Similarly, process claims to disease-correlating biomarkers and diagnostic methods based on such biomarkers had been routinely granted patent rights by the USPTO where the biomarker in question was an identified segment of DNA (Gordon 2015). Such claims often involved the inventor’s identification of a mutant DNA sequence that signified a disease-state or a strong correlation with a given disease (Gordon 2015).

B. Prometheus – Do the Process Claims Add Enough to Qualify as Patent-Eligible Processes that Apply Natural Laws?

In 2012, the Supreme Court took up the question of whether patent claims covering processes that allow doctors to determine optimal doses of certain drugs to treat patients with auto-immune diseases were in fact patent-eligible (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). To address the question, the Court asked whether the patent claims “add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws” (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). The thiopurine drugs at issue were found to be metabolized by different patients at different rates, which could result in ineffective or toxic administration of the drug, depending on the individual’s rate of metabolism (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). The inventors of the claimed process had identified a means of measuring metabolites in the patient’s blood to indicate whether an increase, decrease or no change in the dose of the drug was required (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012).

The Supreme Court concluded that the correlation between the metabolite concentration in the blood and the corresponding need to adjust the dosage was nothing more than “a process

reciting a law of nature" (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). The Court explained that the claimed process lacked "additional features" that would offer some "practical assurance" that the process would not "monopolize the law of nature itself" (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). The *Prometheus* decision does not dictate what criteria biomarker process claims must meet in order to be patent-eligible, but instead warns would-be process inventors that the Court must have some "practical assurance" that the law of nature at issue will not be unduly preempted by conferring a patent on that process claim (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012). This decision gives lower courts a two-step framework for analyzing claims as patent eligible: (1) Is the claim directed to a patent-ineligible concept, i.e. law of nature, natural phenomenon, or abstract idea? and (2) If the answer to the first question is yes, do the limitations of the claim apart from the law of nature or abstract idea – considered individually and as an ordered combination – "transform the nature of the claim into a patent-eligible application" (*Alice Corp. Pty. v. CLS Bank Int'l*, 2014; *Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012)? Unfortunately, the Court offered little guidance as what might constitute this "inventive concept" that transforms a natural product-based claim from patent-ineligible to the patent-eligible (*Prometheus Labs. Inc. v. Mayo Collab. Servs.*, 2012).

C. Not "Enough" = The Identification of Autoantibodies which Bind to a Specific Protein and the Development of a Test Utilizing this Discovery to Diagnose a Disease

Applying the two-step framework of *Prometheus*, the Federal Circuit recently issued a decision concluding that Athena's claimed method for diagnosing *myasthenia gravis* disease was patent-ineligible (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). Athena's test had identified a means of diagnosing *myasthenia gravis* in patients who lack the antibodies that are relied upon to diagnose about 80% of those with the disease (*Athena Diagnostics, Inc. v.*

Mayo Collab. Servs., LLC, 2019). The inventors identified different antibodies which attack a specific protein, MuSK, in the 20% segment of *myasthenia gravis* sufferers who could not be diagnosed with the previously available method (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). These inventors also developed a method of detecting the presence of those antibodies using radioactive iodine, though radioactive labeling of antibodies was not itself a novel tool (*Athena Diagnostics, Inc. v. Mayo Collab. Servs., LLC*, 2019).

In its application of the two-step test from *Prometheus*, the Federal Circuit found that Athena's diagnostic method claims "merely recite observing naturally occurring biological correlations with no meaningful non-routine steps in between" because the correlation between MuSK autoantibodies in bodily fluid and MuSK-related neurological diseases is effectively a natural law (Schaffer, et al. 2019; *Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). The Federal Circuit went on to conclude that the claimed steps for detecting this natural correlation were conventional techniques and thus insufficiently inventive to transform this 'law of nature' into a patent-eligible application of natural law (Schaffer, et al. 2019; *Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019).

Judge Pauline Newman, a dissenting judge to the *Athena Diagnostics, Inc. v. Mayo Collab. Servs., LLC* (hereinafter "Athena Diagnostics") decision, noted that the judges which found the Athena test patent ineligible had misapplied the law – both the statute and legal precedent (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). Judge Newman explained that the Athena test claims sought patent rights for a "multi-step method of diagnosis, not a law of nature" (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). Judge Newman pointed out that none of the steps specific to this diagnostic test had been previously

known, even if the method applied previously known tools of radioactive labeling (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019).

More fundamentally, however, Judge Newman noted that because eligibility is determined for the claim considered as a whole, and the method as a whole functioned to diagnose previously undiagnosable neutrotransmission disorders, the claimed method is directed to a new method of diagnosing *myasthenia gravis*, not to a 'law of nature' (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). Thus the eligibility question should have been readily resolved by answering the first prong of the *Prometheus* inquiry in the negative.

Judge Newman's dissent also highlights the problematic consequences of the majority's decision in *Athena Diagnostics*. Particularly haunting is Judge Newman's cautionary edict that "[t]he loser is the afflicted public, for diagnostic methods that are not developed benefit no one" (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019). Additionally, Judge Newman pointed to the numerous amici curiae who had pleaded with the court for consistency with prior judicial decisions, at a minimum, citing the "unabated uncertainty about the patent-eligibility of many biotechnological inventions" and the adverse impacts such uncertainty has on innovation (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019).

D. Myriad: Was DNA's Information-Carrying Nature Critical to the Decision or is this Case a Patent Law Sea Change Closing the Door to all "Isolated" or "Purified" Product Claims?

In *Myriad*, the Supreme Court held that the isolated DNA sequences for the BRCA1 and BRCA2 genes were not patent-eligible (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). In so concluding, the Court grappled with the question of whether isolated segments of DNA are indeed patent-eligible. Even though the isolation of genes or DNA segments does

indeed involve the breaking of chemical bonds and thus theoretically creates a 'new molecule,' relative to the DNA sequence as it exists within the chromosome, the key to the Court's decision laid in the nature of Myriad's claim (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). The Court was convinced that Myriad was not trying to lay claim to the "creation of a unique molecule" but instead to "the genetic information encoded in the BRCA1 and BRCA2 genes" (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). The claims, as written, were focused not on the chemical composition of these DNA molecules, as contrasted with those found naturally in a human cell, or on how the nature of their isolation changes their purpose or use (as with the adrenaline or vitamin B_{12} examples cited above) but rather with "the information contained in the genetic sequence" (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013).

In the same decision, the Supreme Court held that Myriad's cDNA patents were valid, noting that the key distinction was that Myriad had used extra-cellular technologies to form cDNA, and this was "enough" to remove the molecule from constituting a product of nature (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). But for those who understand how cDNA is made, this distinction seems logically inconsistent with the decision to invalidate Myriad's BRCA1 and BRCA2 gene patents. Explaining its rationale, the Supreme Court noted that "cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived" (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). However, if one applies the same analysis to the DNA, we can say that the DNA retains the natural coding and non-coding regions from the chromosome from which it was extracted but it is equally distinct from its chromosome origin as the cDNA is from the DNA from which it was derived (Tallmadge 2017).

The resolution of this contradiction lies in the information-carrying nature of DNA. The Court's holding was "that genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material" (*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 2013). Understanding that Myriad was trying to monopolize the information of the BRCA gene against others who would try to make use of it, the Court concluded that this claim ran afoul of the bargain of disclosure versus monopoly on which the patent system is founded. Thus, although the USPTO Guidance applies a broad application of this holding, closing the door to all "isolated" or "purified" product claims, it remains to be seen whether the Supreme Court will so expand its holding in *Myriad*. Unfortunately, this uncertainty, by itself, disincentivizes future innovation.

V. Looking Ahead

How can we incentivize more companies to look to the natural world for solutions to pressing health problems if there is a lack of certainty in the diagnostic method and nucleic acid patentability arenas? How can we ensure the patent system strikes a just balance to stimulate this much needed innovation? The law seeks to ensure that new innovations will reach the public domain, hence the disclosure and enablement requirements and limits on patent terms (Johnson 2017; 35 U.S.C. § 112). However, if courts do not consistently interpret and predictably apply these laws to biotechnology claims, won't we see fewer biotechnological innovations? Won't the true "loser," as Judge Newman warns, be the "afflicted public"? (*Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, LLC, 2019).

On the other hand, we must also consider the far-reaching consequences to the "afflicted public" if patents are issued to a wide range of diagnostic methods. Will the public's access to

medical treatment be limited if patent holders to diagnostic methods can exclude such practice? Also, will patent holders to diagnostic methods commence patent infringement suits against doctors? Such policy considerations cannot be removed from the initial patent eligibility question, for the point of the preemption doctrine was to ensure that the basic tools of the field are not monopolized so as to prevent further discoveries and innovations. The key, however, is for the law to ensure foreseeability and certainty in what is patent eligible, even if new statutes must be enacted, because the pursuit of biotechnology research and the therapies that will become available to patients are dependent upon patent predictability.

Case Study Discussion Questions:

1. Is the current state of patent law encouraging or discouraging the innovation of diagnostics, medical treatments and other natural phenomena-based technologies?

2. Should medical diagnostics which rely on natural processes, e.g. protein expression patterns as biomarkers for disease prognosis, be patent-eligible?

3. Where should the line be drawn to determine when a newly-discovered diagnostic method or treatment based on naturally-occurring processes becomes patent-eligible?

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U.S. Const. art. I, § 8, cl. 8.

28 U.S.C. § 1295.

28 U.S.C. § 1338(a).

35 U.S.C. §§1, 2.

35 U.S.C. § 101.

35 U.S.C. §154(a).