THE SHAPE OF THINGS TO COME: A COHESIVE APPROACH TO PATENT-ELIGIBLE SUBJECT MATTER AND BIOTECHNOLOGY

INTRODUCTION

Our society has made remarkable advances in medical science over the past few decades. A significant portion of these advances has resulted from the sizable research and development investments made into a seemingly ever-growing biotechnology industry.[1] Unsurprisingly, biotechnology entities rely heavily on patent protection to recoup research and development costs before competitors can introduce similar products into the market.[2] The desire for prolific patent portfolios is increasing, and without strong patent protection, biotechnology startups are likely to fail.[3]

But, the current legal system cannot match the speed with which biotechnology is developing. More specifically, the current analytical framework for determining patent-eligible subject matter under 35 U.S.C. § 101 has become unworkable in the face of these emerging technologies. Further, the case law provides no clear prefiling guidance for biotechnology that walks the fine line between science as it is found in nature and science as it is developed by man.

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1. *See* John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 101, 136–41 (2001) (discussing the various means of securing investments for biotechnology research and the billions of dollars annually invested).

2. *See* Jerzy Koopman, *The Patentability of Transgenic Animals in the United States of America and the European Union: A Proposal for Harmonization*, 13 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 103, 117–18 (2002) ("Patents . . . enabl[e] the inventor to recover a profit for a period of time in which he or she retains exclusivity for this invention."); John W. Schlicher, *If Economic Welfare Is the Goal, Will Economic Analysis Redefine Patent Law?*, 4 J. PROPRIETARY RTS. 12, 12 (1992) ("[A] free market economy will not provide adequate incentives to produce the right kinds of technical information at the right times, unless the law provides patent rights."); Elaine Stracker, Hewlett-Packard Co. v. Repeat-O-Type Stencil Manufacturing Corp., 13 BERKELEY TECH. L.J. 175, 191–92 (1998) ("Patent law . . . provides the incentive to invest in and produce new technology.").

3. *See* Stuart J.H. Graham et al., *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 24 BERKELEY TECH. L.J. 1255, 1280 (2009) (quoting a venture capitalist as saying, "When you go into life sciences . . . if it doesn't have a reasonably strong patent, and if you don't have the capability to expand the patent estate covering your technology and products, you are going to have complicating issues").

Two recent Supreme Court decisions, *Mayo Collaborative Services v. Prometheus Labs, Inc.*[4] and *Association for Molecular Pathology v. Myriad Genetics, Inc.*,[5] have addressed the threshold determination of patentable subject matter under § 101.[6] However, no cohesive approach to patentable subject matter has been articulated following these two cases, increasing uncertainty for drafters and litigators of biotechnology patent claims. Some scholars argue that the Supreme Court continually focuses too much on textual analysis to determine patentable subject matter, neglecting to consider the promotion or progress in the useful arts as required by the constitutional mandate.[7]

Ambiguity is intensified by the U.S. patent system's structure, which historically has prevented challenges to the validity of a patent "until after a patent is used and then relies on the reexamination process."[8] An issued patent affords a strong presumption of validity that can only be defeated by clear and convincing evidence.[9] Moreover, because the patent remains in full force during the reexamination and appeals process, this post hoc approach may encourage the patent holder to actively assert exclusivity rights and bolster his or her patent domain.[10] Indeed, the mantra seems to be "patent first, ask questions later."[11]

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4. 132 S. Ct. 1289 (2012).

5. 133 S. Ct. 2107 (2013).

6. *See generally Myriad*, 133 S. Ct. 2107; *Mayo*, 132 S. Ct. 1289.

7. Peter S. Menell, *Forty Years of Wondering in the Wilderness and No Closer to the Promised Land:* Bilski*'s Superficial Textualism and the Missed Opportunity to Return Patent Law to Its Technology Mooring*, 63 STAN. L. REV. 1289, 1313–14 (2011) ("The Supreme Court's textualist turn has worked a great disservice to the promotion of progress in the useful arts and preserving free enterprise.").

8. Aurora Plomer et al., *Challenges to Human Embryonic Stem Cell Patents*, 2 CELL STEM CELL 13, 13 (2008). However, the America Invents Act now provides for post-grant review whereby a third party may challenge a patent issued by the USPTO within nine months of the patent grant. 35 U.S.C. § 321 (2012). Post-grant review will only be available for patents having an effective filing date of March 16, 2013, or later. *Post Grant Review*, U.S. PAT. & TRADEMARK OFF., http://www.uspto.gov/aia_implementation/faqs_post_grant_review.jsp (last modified Dec. 11, 2013).

9. 35 U.S.C. § 282 (2012) ("A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims."); *see* Sciele Pharma Inc. v. Lupin Ltd., 684 F.3d 1253, 1259–60 (Fed. Cir. 2012) (holding that the presumption of validity extends to all issued claims, even when the USPTO mistakenly issued the claims); *see also* David W. Okey, *Issued Patents and the Standard of Proof: Evidence Clear and Convincing or Merely Ponderous?*, 17 J. MARSHALL J. COMPUTER & INFO. L. 557, 558 (1999) (discussing the evidentiary standard for invalidating a patent).

10. *See* Plomer et al., *supra* note 8, at 14. According to one data compilation for filing dates between 1981 and 2007, reexaminations initiated by third parties only result in cancellation of the entire patent twelve percent of the time, while twenty-nine percent of reexaminations result in a confirmation

The "lack of a forthright, principled framework for delineating the boundaries of patentable subject matter" has caused investors and inventors alike to seek expansive patent portfolios.[12] Given the recent proliferation of validity challenges, their rights are anything but secure.[13] Industry players may manipulate the current framework to cover as much intellectual property as possible in the event their claims are later dismantled by invalidating court decisions and declaratory judgments.[14]

The Supreme Court insists that patent eligibility cannot "depend simply on the draftsman's art."[15] But, the legal framework seems to assiduously depend on a "doctrine of magic words" whereby patentable subject matter is determined by the applicant's recitation of key phrases and placement of terminology.[16] Thus, if patents are to survive post hoc challenges, words that delineate the claims must be chosen and construed carefully at the prefiling stage.

As a solution to industry-wide uncertainty, I suggest a threefold approach, referred to as the Triangle Method, which can serve as a useful guide for drafters and litigators based on the Supreme Court's recent line of § 101 cases. The three complementary sides of the triangle are: (1) inventiveness, (2) structural differences, and (3) informational or functional differences.[17] Under this framework, a

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of the entire patent and fifty-nine percent result in confirmation with modification to the claims. *Id.* Of course, the high confirmation rates are largely a result of patent holders initiating fifty percent of reexaminations themselves in order to reinforce their patent claims. *Id.*

11. Margo A. Bagley, *Patent First, Ask Questions Later: Morality and Biotechnology in Patent Law*, 45 WM. & MARY L. REV. 469, 494 (2003).

12. Menell, *supra* note 7, at 1305–07, 1313–14.

13. *See* John R. Allison et al., *Understanding the Realities of Modern Patent Litigation*, 92 TEX. L. REV. 1769, 1785, 1800–01 (2014) (examining data to determine whether patentable subject matter motions for summary judgment prevail a majority of the time and that "the most successful validity challenges today—patentable subject matter and indefiniteness—were virtually unknown twenty years ago").

14. *See* Robert P. Merges, *As Many As Six Impossible Patents Before Breakfast: Property Rights for Business Concepts and Patent System Reform*, 14 BERKELEY TECH. L.J. 577, 586 (1999) ("Patent lawyers, paid to push the outer limits of what is protectable, have responded to the new technological realities with remarkable creativity."); *see also* Golden, *supra* note 1, at 133 ("[A] natural tendency of industry players is to seek to increase cumulative intellectual property protection, whether by patenting inventions indiscriminately or by lobbying Congress for even more relaxed standards of patentability.").

15. Alice Corp. Pty. Ltd. v. CLS Bank Int'l, No. 13-298, slip op. at 16 (U.S. June 19, 2014) (quoting Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294 (2012)).

16. Julie E. Cohen & Mark A. Lemley, *Patent Scope and Innovation in the Software Industry*, 89 CALIF. L. REV. 1, 9 (2001) (coining the "doctrine of magic words" in the context of computer software patents).

17. Factors (2) and (3) are slightly conflated in the Supreme Court's *Myriad* decision due to the nature of the claims at issue in that case; however, they must remain separate for a cohesive framework, as explained *infra* Part III.

patent that satisfies all three sides of the triangle is more easily defended against future challengers seeking to invalidate the patent as ineligible subject matter. The Triangle Method thus provides predictability in the event of patent invalidation suits and, in turn, increases the dependability of our patent system as a whole.

Instead of engaging in the rich, ongoing academic debate over necessary legislative amendments or alternative intellectual property systems for adequate protection of emerging biotechnologies,[18] I have chosen a method that works within the current patentable subject matter framework. Instead of hypothesizing over what we *should* do with regard to patentable subject matter and biotechnology, it is better to work with the realistic premise of what we *are* doing.[19] It is more likely that the law will simply mirror its previous response to inventive industries that have outpaced legal developments[20] by forcing the current patent law to accommodate rapidly emerging biotechnology advancements.

This Note introduces the recent and remarkable report of cellular reprograming called stimulus-triggered acquisition of pluripotency ("STAP") in Part I to illustrate the future direction of biotechnology and the § 101 issues that will necessarily arise. Part II demarcates the analytical framework for patentable subject matter as it relates to biotechnology following the recent Supreme Court decisions in *Mayo* and *Myriad*. Part III sets forth the

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18. *See* Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1576–77 (2003) (discussing the flaws of current patent law as applied to emerging technologies); Mark A. Lemley et al., *Life After* Bilski, 63 STAN. L. REV. 1315, 1326–27 (2011) (arguing that the "gatekeeping" approach of current patent law has "proven unsatisfactory"); Simone A. Rose, *Semiconductor Chips, Genes, and Stem Cells: New Wine for New Bottles?*, 38 AM. J.L. & MED. 113, 114 (2012) (arguing for "*sui generis* (of its own class) intellectual property protection for isolated bioproducts"); Allen K. Yu, *Within Subject Matter Eligibility—A Disease and a Cure*, 84 S. CALIF. L. REV. 387, 387 (2011) (discussing the shortcomings of current patent law in the biomedical context); *see also* ORG. FOR ECON. CO-OPERATION AND DEV., GENETIC INVENTIONS, INTELLECTUAL PROPERTY RIGHTS AND LICENSING PRACTICES: EVIDENCE AND POLICIES 31–32 (2002), *available at* http://www.oecd.org/dataoecd/42/21/2491084.pdf (explaining the pros and cons of various reform suggestions).

19. This distinction between "is" and "ought" is most famously derived from DAVID HUME, TREATISE OF HUMAN NATURE 469 (Prometheus Books 1992) (1738).

20. *See, e.g.*, Cohen & Lemley, *supra* note 16, at 5 (explaining that the patent world can adapt for computer software creation that "is characterized by rapid sequential innovation"); Chris Strobel, *Wind Power and Patent Law: How the Enforcement of Wind Technology Patents May Lead to Restricted Implementation in the US, and Necessary Solutions*, 19 J. ENVTL. & SUSTAINABILITY L. 501, 502 (2013) (explaining how the patent law has quickly responded to emerging wind technology patents). *But see generally* Rose, *supra* note 18 (explaining the benefits of a *sui generis* intellectual property system for biotechnology and providing a valuable comparison to the semiconductor technology *sui generis* system).

proposed Triangle Method as a framework for drafters and litigators in order to strengthen the validity of biotechnology patent claims against § 101 challenges. Finally, the value of the Triangle Method is illustrated in Part IV by applying the framework to the STAP cell problem.

I. STAP CELLS: AN EXAMPLE OF PATENT-ELIGIBLE SUBJECT MATTER DIFFICULTIES

In January 2014, researchers at Brigham and Women's Hospital, in collaboration with the Japanese Riken Center for Developmental Biology, and led by Dr. Haruko Obokata, determined[21] that mature, adult cells have the potential to revert into a state of pluripotency when exposed to external forces such as trauma, low oxygen environments, and acidic environments.[22] The

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21. Since the drafting of this Note, there has been significant controversy surrounding the scientific validity of Obokata's findings, ultimately resulting in the retraction of the two high-profile papers in the journal *Nature*. *See, e.g.*, David Cyranoski, *Papers on "Stress-Induced" Stem Cells Are Retracted*, NATURE (July 2, 2014), http://www.nature.com/news/papers-on-stress-induced-stem-cells-are-retracted-1.15501; Kanoko Matsuyama & Kiyotaka Matsuda, *Riken Apologizes for Errors in Two Stem Cell Studies*, BLOOMBERG (Mar. 14, 2014, 6:59 AM), http://www.bloomberg.com/news/2014-03-14/riken-apologizes-for-errors-in-two-stem-cell-studies.html. But the validity of these findings is essentially immaterial to this Note's purpose. The product and method in question merely serve to illustrate the future direction of scientific research, the difficulties of the current patentability analysis, and the usefulness of the Triangular Method proposed herein.

22. Haruko Obokata et al., *Stimulus-Triggered Fate Conversion of Somatic Cells into Pluripotency*, 505 NATURE 641, 641 (2014) [hereinafter Obokata et al., *Stimulus-Triggered Fate Conversion*]; *see also Acid Shock Converts Adult Cells to Stem Cells*, GEN (Jan. 29, 2014), http://www.genengnews.com/gen-news-highlights/acid-shock-converts-adult-cells-to-stem-cells/81249434/ (providing general overview of STAP cell research methods and results); *Researchers Create Embryonic Stem Cells Without Embryo*, PHYS.ORG (Jan. 29, 2014), http://phys.org/news/2014-01-embryonic-stem-cells-embryo.html (same). One of the two articles published by the researchers also indicates the potential for totipotency based on mice studies; however, the findings remain focused on the cells' pluripotent characteristics. Haruko Obokata et al., *Bidirectional Developmental Potential in Reprogrammed Cells with Acquired Pluripotency*, 505 NATURE 676, 679 (2014) [hereinafter Obokata et al., *Bidirectional Developmental Potential*]. "Totipotent stem cells are capable of producing all tissue, including the trophoblast necessary for implementation," which indicates the potential to develop into an embryo. TED PETERS, SCIENCE, THEOLOGY, AND ETHICS 184 (2003). Pluripotent cells, on the other hand, have every capability of the totipotent stem cells while lacking the trophoblast. *Id.* In other words, without the trophoblast, pluripotent cells cannot develop into full human beings; as such, pluripotent cells are not potential embryos. *Id.*; *see also* Helen Thomson, *Extraordinary Stem Cell Method Tested in Human Tissue*, NEW SCIENTIST (Feb. 5, 2014, 7:24 PM), http://www.newscientist.com/article/dn25004-extraordinary-stem-cell-method-tested-in-human-tissue.html (explaining that pluripotent cells "can form into any cell in an embryo but not a placenta," whereas totipotent cells "can form any cell in an embryo and

researchers refer to this novel and unique adult cell reprogramming as stimulus-triggered acquisition of pluripotency.[23] The notion of pluripotency refers to "the potential of a particular cell to develop into all cell types found in the embryonic and adult organism."[24] Embryonic stem cells are naturally pluripotent, which allows scientists to direct their adult form and constitutes the prime reason that embryonic stem cell research is so coveted.[25] Adult stem cells, on the other hand, are not naturally pluripotent.[26] Instead, they are considered multipotent, which means they are limited to differentiating only into a particular cell type or types, usually the tissue type from which they were pulled.[27]

Obokata's method reverts the adult cells to an embryonic-like pluripotent state without touching the DNA and without necessitating cell division.[28] This method may allow researchers to one day create cells specific to each individual through a simple skin biopsy or blood sample.[29] The cells could then be used to create patient-specific tissue without needing to manipulate naturally present genes or insert any outside genetic material.[30] Moreover, Obokata's process converted seven to nine percent of the original cells into STAP cells, which is more effective than the one percent

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placenta—meaning they have the potential to create life"). Heretofore, the only cells known to be naturally totipotent are in embryos having experienced the first stages of cell division following fertilization. *Id.*

23. *Researchers Create Embryonic Stem Cells Without Embryo*, *supra* note 22.

24. HUMAN STEM CELL TECHNOLOGY AND BIOLOGY: A RESEARCH GUIDE AND LABORATORY MANUAL 141 (Gary S. Stein et al. eds., 2011).

25. Sherley v. Sebelius, 776 F. Supp. 2d 1, 4–5 (D.D.C. 2011), *aff'd*, 689 F.3d 776 (D.C. Cir. 2012).

26. *Researchers Create Embryonic Stem Cells Without Embryo*, *supra* note 22.

27. Jenny Shum, Note, *Moral Disharmony: Human Embryonic Stem Cell Patent Laws, WARF, and Public Policy*, 33 B.C. INT'L & COMP. L. REV. 153, 155 (2010).

28. Obokata et al., *Stimulus-Triggered Fate Conversion*, *supra* note 22, at 641–42. Creating STAP cells is more direct than creating induced pluripotent stem ("iPS") cells, and STAP cells damage less of the original cell's genetic material. *Global Patent War Looms with Epoch-Making Discovery of STAP Cells*, ASAHI SHIMBUN (Feb. 3, 2014), http://ajw.asahi.com/article/behind_news/social_affairs/AJ201402030077; *see also* Monte Morin, *New Method Makes Stem Cells in About 30 Minutes, Scientists Report*, L.A. TIMES (Jan. 29, 2014, 1:03 PM), http://www.latimes.com/science/sciencenow/la-sci-sn-stap-stem-cells-20140129,0,517478.story#axzz2tIk88CUN (explaining that the "simpler, cheaper and faster" STAP method involves a "reprogramming" period of only thirty minutes).

29. *Researchers Create Embryonic Stem Cells Without Embryo*, *supra* note 22.

30. Alexander Martin, *Japanese Scientists to Offer More Details on Stem-Cell Work*, WALL ST. J. ONLINE (Feb. 21, 2014, 4:38 AM), http://onwsj.com/12VydpO.

conversion rate provided by previously utilized methods.[31] The process thus provides a more cost-effective and efficient transformation process than previously known.[32]

The patenting process to claim Obokata's STAP cell–creation technique began in April 2012, before the official announcement of the discovery.[33] The patent "relates to methods, assays, and compositions relating to causing a cell to assume a more pluripotent state, e.g., without introducing foreign genetic material."[34] With patent protection pending, the issue is whether STAP cells or the process by which they are created constitute a "new and useful process . . . or composition of matter."[35]

The crux of the problem lies in the researchers' emphasis on the absence of genetic manipulation and the absence of added genetic material. Researchers describe the process as activating unknown cellular functions through external stressors,[36] and this statement alone indicates the activated cellular functions would be preexisting and not newly *created*.[37] Moreover, the creation process itself sits in a precarious position. The process is new in the sense that scientists did not previously expose adult stem cells to external stressors in order to invoke a pluripotent state.[38] But, if the process is viewed narrowly, the adult cell's ability to revert has always been naturally present because adult stem cells have the innate capacity to revert in instances of trauma.[39]

As a result, STAP cells lie in a purgatory of patent-eligible subject matter. STAP cells themselves have never before been created by man, but their pluripotent characteristics have been

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31. Morin, *supra* note 28. The first person to produce iPS cells and winner of a Nobel Prize in 2012 for his work, Dr. Shinya Yamanaka's reprogramming process converts only about one percent of the cells into iPS, and clinical studies continue to assess the cells' long-term stability and safety. *Id.*

32. Thomson, *supra* note 22.

33. U.S. Patent Application No. 61/637,631 (filed Apr. 24, 2012) (noting April 24, 2012, as the priority date), *available at* http://patentscope.wipo.int/search/docservicepdf_pct/id00000022883817.pdf; *see also Global Patent War Looms with Epoch-Making Discovery of STAP Cells*, *supra* note 28 (reporting that preparations for patent filing were underway two years before the discovery was made public).

34. '631 Patent Application, *supra* note 33, at 1.

35. 35 U.S.C. § 101 (2012).

36. *Researchers Create Embryonic Stem Cells Without Embryo*, *supra* note 22.

37. *See Interview with Charles Vacanti on STAP Cells: Link to Spore Stem Cells & More*, KNOEPFLER LAB STEM CELL BLOG (Feb. 2, 2014), http://www.ipscell.com/2014/02/interview-with-charles-vacanti-on-stap-cells-link-to-spore-stem-cells-more/ [hereinafter *Vacanti Interview*] ("Our primary desire was to shed light on what we felt was a previously unrecognized biological phenomenon that causes mature cells to revert to stem cells.").

38. *Id.*

39. *Id.*

created by Mother Nature in the event of trauma.[40] Therefore, the subject matter eligibility issue turns on a nuanced characterization: the discovery of an adult stem cell with pluripotent capabilities versus the recreation of pluripotency in naturally multipotent adult stem cells.[41]

II. LEGAL BACKGROUND: BIOTECHNOLOGY AND § 101

The statutory foundation for patent-eligible subject matter, 35 U.S.C. § 101, provides that patent protection may only be secured for a "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[42] In contrast, patent claims directed to laws of nature, natural phenomena, or abstract ideas are not patent eligible.[43] While several major cases have fleshed out these requirements and limitations over the years,[44] this Note will focus on case law related to inventions in the life sciences industry that challenges the prohibition on patenting laws of nature and natural phenomenon.

The two recent Supreme Court cases addressing biotechnology and § 101 patent-eligible subject matter are *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* and *Association for Molecular Pathology v. Myriad Genetics, Inc.* Both cases presented the Court with issues of first impression.[45] While the former pertains to method claims and the latter pertains to composition claims,[46] the two cases in combination provide the current legal

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40. *Id.*

41. *See* Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("[A] patentee may choose to be his own lexicographer"); *see also* Atlantic & Gulf Stevedores, Inc. v. Kominers, 456 F.2d 1146, 1149 (2d Cir. 1972) ("In short, lawyers are supposed to be wordsmiths.").

42. 35 U.S.C. § 101 (2012).

43. Diamond v. Diehr, 450 U.S. 175, 185 (1981); Gottschalk v. Benson, 409 U.S. 63, 67–68 (1972).

44. *See generally* Bilski v. Kappos, 561 U.S. 593 (2010); Diamond v. Chakrabarty, 447 U.S. 303 (1980); Parker v. Flook, 437 U.S. 584 (1978); Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948); O'Reilly v. Morse, 56 U.S. (15 How.) 62, 112–20 (1853); Dealertrack, Inc. v. Huber, 674 F.3d 1315 (Fed. Cir. 2012); Research Corp. Tech., Inc. v. Microsoft Corp., 627 F.3d 859, 868 (Fed. Cir. 2010); State St. Bank & Trust Co. v. Signature Fin. Grp., Inc., 149 F.3d 1368 (Fed. Cir. 1998).

45. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2111 (2013); Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294 (2012).

46. The Supreme Court did not address Myriad's method claims on appeal. *Myriad*, 133 S. Ct. at 2119. Below, the Federal Circuit concluded that the method of screening potential cancer therapeutics by changes in transformed host cell growth rates is eligible for patent protection because the method is based on the use of man-made host cells. Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1336 (Fed. Cir.), *cert. granted in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 694 (2012), *aff'd in part, rev'd in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics,

landscape for biotechnology and patent-eligible subject matter. The combination is especially significant where claimed methods and compositions are often significantly intertwined.[47]

A. Mayo Collaborative Services v. Prometheus Laboratories, Inc.

In *Mayo*, the Court held that the claimed use of thiopurine drugs to treat autoimmune diseases did not constitute patent-eligible subject matter.[48] Prometheus Laboratories' ("Prometheus") patents recited the discovered correlations between patients' blood metabolite levels and the likely harm or ineffectiveness of the thiopurine drugs.[49] This correlation formed the basis for Prometheus's claimed diagnostic test.[50] Mayo Collaborative Services ("Mayo") utilized a similar diagnostic test and Prometheus sued for infringement.[51]

The district court concluded that Mayo's test infringed Prometheus's patents, but granted summary judgment to Mayo because the claimed processes were natural laws or natural phenomena.[52] In other words, the patents were not valid in the first place, so infringement could not have logically occurred.[53] On appeal, the Federal Circuit reversed, holding that the processes were patentable subject matter under the infamous "machine or transformation test."[54] When the Supreme Court first took the

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Inc., 133 S. Ct. 2107 (2013). However, the method of comparing or analyzing DNA sequences is ineligible for patent protection because it covers only an abstract mental process. *Id.* at 1335.

47. Stephen R. Munzer, *The Special Case of Property Rights in Umbilical Cord Blood for Transplantation*, 51 RUTGERS L. REV. 493, 542 (1999); *see also* Bandag, Inc. v. Al Bolser's Tire Stores, Inc., 750 F.2d 903, 922 (Fed. Cir. 1984) ("It is commonplace that the claims defining some inventions can by competent draftsmanship be directed to either a method or an apparatus."). The interconnection's economic importance is evidenced by Myriad's stock price drop following the Supreme Court's decision despite the continued validity of its method claims. Susan Decker, *Myriad Falls After Losing Bid to Block Competing Tests*, BLOOMBERG (Mar. 11, 2014, 4:19 PM), http://www.bloomberg.com/news/2014-03-11/myriad-falls-after-losing-bid-to-block-competing-tests.html.

48. *Mayo*, 132 S. Ct. at 1294.

49. U.S. Patent No. 6,680,302 (filed Dec. 27, 2001), *available at* http://patft.uspto.gov/netahtml/PTO/srchnum.htm (query "6680302"); U.S. Patent No. 6,355,623 (filed Apr. 8, 1999), *available at* http://patft.uspto.gov/netahtml?PTO/srchnum.htm (query "6355623"); *see also Mayo*, 132 S. Ct. at 1294–95.

50. *Mayo*, 132 S. Ct. at 1294.

51. *Id.* at 1295–96.

52. *Id.* at 1296.

53. 35 U.S.C. § 282(b)(2) (2012).

54. Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d 1336, 1345 (Fed. Cir. 2009) *cert. granted, judgment vacated*, 130 S. Ct. 3543 (2010). The "machine or transformation test" provides that a patent applicant may prove patent-eligible subject matter "either by showing that his claim is tied to a particular machine" or by showing that "it transforms an article into a

appeal, it remanded the case for reconsideration in light of *Bilski v. Kappos*,[55] wherein the Court firmly explained that the "machine or transformation test" is not the sole and determinative test for § 101 patentable subject matter.[56] The Federal Circuit then reaffirmed its finding of patent ineligibility on remand.[57]

The Supreme Court granted certiorari and held that Prometheus's claimed process was not patent eligible.[58] The issue was framed as whether the claims go beyond merely describing the operative principles of natural law and add enough to the discovered metabolite-effectiveness correlation in order to qualify as patent-eligible subject matter.[59] The Court reasoned that the concentrations of the metabolites in the blood and the patient's reaction are not themselves patentable because they exist naturally, with or without scientific interaction.[60] The claimed processes did not become patent eligible simply because they were discovered.[61] Patent eligibility would only have been available if Prometheus had set forth new steps for the application of those natural processes.[62]

Although the patent attempted to recite additional steps, those steps were insufficient to constitute a patent-eligible application.[63] The three additional steps were described as the "administering," "wherein," and "determining" steps.[64] The "administering" step attempted to limit the formula's use to a particular set of patients.[65] However, doctors had already been using the drugs for this patient population long before Prometheus's patent, so the step was not inventive.[66] The "wherein" step merely suggested that doctors consider test results in relation to the relevant natural laws when treating patients, and thus also failed to add an inventive aspect to the natural correlation.[67] Finally, the "determining" step instructed doctors to measure a patient's metabolite levels without prescribing

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different state or thing." *In re* Bilski, 545 F.3d 943, 961–62 (Fed. Cir. 2008), *aff'd sub nom.* Bilski v. Kappos, 130 S. Ct. 3218 (2010).

55. 130 S. Ct. 3218 (2010).

56. *Mayo*, 132 S. Ct. at 1296; *Bilski*, 130 S. Ct. at 3226.

57. Prometheus Labs., Inc. v. Mayo Collaborative Servs., 628 F.3d 1347, 1355 (Fed. Cir. 2010), *rev'd*, 132 S. Ct. 1289 (2012).

58. *Mayo*, 132 S. Ct. at 1297.

59. *Id.* at 1294.

60. *Id.* at 1296–97.

61. *Id.* at 1294.

62. *Id.* at 1297.

63. *Id.* at 1298 (citing Parker v. Flook, 437 U.S. 584, 590 (1978)).

64. '623 Patent, *supra* note 49, at col. 20 l. 10–24; *see also Mayo*, 132 S. Ct. at 1297.

65. *Mayo*, 132 S. Ct. at 1297.

66. *Id.* (citing Bilski v. Kappos, 130 S. Ct. 3218, 3230 (2010)) (explaining that the "prohibition against patenting abstract ideas cannot be circumvented by attempting to limit the use of the formula to a particular technological environment." (internal quotation marks omitted)).

67. *Id.*

a specific process.[68] Like the previous two steps, this merely directed doctors to engage in "well-understood, routine, [and] conventional" practices and remained unpatentable.[69]

Even considering the additional steps as a whole, the Court concluded that Prometheus failed to add any element of inventiveness that was not already present when the steps were considered separately.[70] Thus, the claimed method could not be considered a "new and useful process" for purposes of § 101 patent eligibility.

The Court cited *Diamond v. Diehr*[71] and *Parker v. Flook*[72] to reinforce the principle that natural processes, like the laws of nature themselves, are not patentable.[73] In *Diehr*, the claimed method for molding rubber based on a mathematical equation—a law of nature—was nevertheless patent-eligible subject matter because additional steps successfully integrated the equation into a larger, useful process.[74] The larger *Diehr* process provided "an inventive application of the formula."[75] In *Flook*, however, the claimed methods for updating alarm limits based on a natural algorithm were so "well known" in the industry that the purported application method provided no "inventive concept."[76] Therefore, the processes could not pass § 101 muster. Based on the rule and reasoning in *Diehr* and *Flook*, the Court concluded in *Mayo* that Prometheus's steps added no "inventive" aspect to the activity in which the industry was previously engaged.[77]

Building off of these concepts, the Court also expressed its concern that patent law should encourage, not inhibit, scientific development.[78] Because laws of nature are "the basic tools of scientific and technological work," the Court explained that patenting discoveries without more could tie up the use of nature.[79] Patented processes that merely articulate general instructions to "apply the natural law" threaten to stifle the development of better testing processes that would springboard off of these basic principles.[80] The inventor "must do more than simply state the law of nature while adding the words 'apply it'" in order to "transform an

68. *Id.*
69. *Id.* at 1298.
70. *Id.*
71. 450 U.S. 175 (1981).
72. 437 U.S. 584 (1978).
73. *Mayo*, 132 S. Ct. at 1298–1300.
74. *Diehr*, 450 U.S. at 177–79, 187.
75. *Mayo*, 132 S. Ct. at 1299.
76. *Flook*, 437 U.S. at 594.
77. *Mayo*, 132 S. Ct. at 1299–1300.
78. *Id.* at 1301.
79. Gottschalk v. Benson, 409 U.S. 63, 67 (1972).
80. *Mayo*, 132 S. Ct. at 1301.

unpatentable law of nature into a patent-eligible *application* of such a law."[81]

However, the Court recognized that to discredit "*all* laws of nature when evaluating a patent application . . . would 'make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious.'"[82] Therefore, the *Mayo* framework seeks to find the appropriate balance between limitations on patent-eligible subject matter and the use of the most foundational concepts necessary for scientific progress. But, its directions are not precise, and following the Court's decision, doctrinal gaps remained.

B. Association for Molecular Pathology v. Myriad Genetics, Inc.

In *Myriad*, a variety of medical patients, advocacy groups, and doctors sought a declaratory judgment against Myriad Genetics, Inc. ("Myriad"), a research laboratory, to render invalid its patents for isolated deoxyribonucleic acid ("DNA") and man-made composite DNA ("cDNA").[83] With its patents in force, Myriad had the exclusive right to develop medical tests for detecting DNA mutations known to increase the risk of ovarian and breast cancers.[84] These mutations are known as BRCA1 and BRCA2 sequences.[85] Myriad isolated the mutations and synthetically created cDNA containing a companion amino acid sequence to be used for assessing a patient's cancer risk.[86]

The district court determined that Myriad's composition claims for the isolated DNA and man-made cDNA were invalid under § 101.[87] The Federal Circuit reversed on appeal,[88] but the Supreme Court vacated the judgment and remanded the case for the Federal Circuit to consider the claims in light of the *Mayo* decision.[89] On remand, the Federal Circuit upheld the validity of the claims for both the isolated DNA and man-made cDNA.[90] The Federal Circuit

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81. *Id.* at 1294.

82. *Id.* at 1304 (quoting Diamond v. Diehr, 450 U.S. 175, 189 n.12 (1981)).

83. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2111, 2114 (2013).

84. *Id.* at 2112–13.

85. *Id.* at 2112.

86. *Id.* at 2112–13.

87. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 220 (S.D.N.Y. 2010), *aff'd in part, rev'd in part*, 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

88. Ass'n for Molecular Pathology v. USPTO, 653 F.3d 1329, 1334 (Fed. Cir. 2011), *vacated, appeal reinstated*, 467 F. App'x 890 (Fed. Cir. 2012).

89. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794, 1794 (2012).

90. Ass'n for Molecular Pathology v. USPTO, 689 F.3d 1303, 1337 (Fed. Cir. 2012), *aff'd in part, rev'd in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

also upheld the method claims for screening potential cancer therapeutics through monitoring changes in cell growth rates.[91] However, the court struck down the method claim for comparing the isolated DNA sequences' association with predisposition for the cancers.[92]

On appeal, the Supreme Court analyzed composition Claims 1, 2, 5, and 6 from Myriad's U.S. Patent 5,747,282 ("the '282 patent").[93] Claim 1 covered the isolated DNA portion that directs production of the BRCA1 and BRCA1 mutations.[94] Claim 2 covered the cDNA nucleotide sequence designed to code for the specific amino acid sequence associated with the BRCA mutations.[95] Claim 5 claimed a segment of the information contained in Claim 1—any 15-nucleotide-long strand of isolated DNA that mimics a series of nucleotides in the typical BRCA1 gene.[96] Similarly, Claim 6 sought to cover a segment of genetic information contained in Claim 2[97]—a 15-nucleotide-long portion that mimics the series of nucleotides as they are found in the man-made cDNA.[98]

The Court unanimously held that the isolated DNA segment in Claim 1 was not patent-eligible subject matter under § 101.[99] Although Myriad discovered the importance and utility of the gene mutations through isolation, it did not create or alter any aspect of the genetic material.[100] It did not affect the genetic information encoded in the genes, and it did not affect the genetic structure of the DNA.[101] Moreover, it did not affect the location or order of the genetic sequences as they existed in nature prior to isolation.[102] Therefore, because the patent sought to claim the natural mutation itself without adding anything new or useful, it was patent-ineligible subject matter under § 101.[103]

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91. *Id.*
92. *Id.*
93. *Myriad*, 133 S. Ct. at 2113 (2013); U.S. Patent No. 5,747,282 (filed June 7, 1995), *available at* http:patft.uspto.gov/netahtml/PTO/srchnvm.htm (query "5747282"). Because the Court did not address Myriad's method claims, the Federal Circuit's opinion stands with regard to Claim 1 of Myriad's U.S. Patent 5,709,999 and U.S. Patent 5,710,001, as well as Claims 1 and 2 of Myriad's U.S. Patent 6,033,857. *See Ass'n for Molecular Pathology*, 689 F.3d at 1333 (holding the claims to be patent-ineligible subject matter because they claimed only abstract mental processes), *aff'd in part, rev'd in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).
94. '282 Patent, *supra* note 93, at col. 153 l. 57–59.
95. *Id.* at col. 153 l. 60–61.
96. *Id.* at col. 153 l. 66–67.
97. *Id.* at col. 154 l. 55–56.
98. *Id.*
99. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2110–11 (2013).
100. *Id.* at 2116, 2118.
101. *Id.* at 2116.
102. *Id.*
103. *Id.* at 2117–18.

The cDNA, on the other hand, was held to be patent eligible.[104] While the cDNA contained amino acids that were common to naturally occurring DNA, Myriad removed the genetic codes for all other naturally occurring genetic components.[105] "[T]he lab technician unquestionably creates something new" by selectively removing portions of genetic information and retaining others.[106] Thus, because the patent sought to claim a product unavailable in nature, the cDNA was deemed patent-eligible subject matter.[107]

In its analysis, the Court addressed *Diamond v. Chakrabarty*[108] and *Funk Brothers Seed Co. v. Kalo Inoculant Co.*[109] In *Chakrabarty*, the Court held that a man-made, genetically engineered bacteria capable of breaking down multiple components of crude oil was patent-eligible subject matter.[110] The bacteria was patent eligible because it was "a product of human ingenuity" and had "markedly different characteristics" from naturally occurring bacteria.[111] In contrast, Myriad's Claim 1 failed to actually "create anything" like the bacteria inventors in *Chakrabarty*.[112] Although Myriad "found an important and useful gene," the act of "separating that gene from its surrounding genetic material is not an act of invention."[113]

The bacteria in *Funk Brothers*, on the other hand, was not patent eligible because the composition was identical to the composition found in nature.[114] The patent claimed a particular mix of bacteria strains that allowed leguminous plants to fixate nitrogen without the different strains inhibiting each other.[115] The Court explained that the collection of naturally occurring bacteria "was not the product of invention" but rather a mere "discovery of the phenomena of nature."[116] Therefore, § 101 prohibited patenting the bacteria composition that simply "serve[d] the ends nature originally provided and act[ed] quite independently of any effort of the patentee."[117]

The reasoning in *Funk Brothers* is directly applicable to Myriad's isolated DNA in Claim 1. Because the isolated DNA served the ends that nature originally provided, and those ends

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104. *Id.* at 2111.
105. *Id.* at 2119.
106. *Id.*
107. *Id.* at 2111.
108. 447 U.S. 303 (1980).
109. 333 U.S. 127 (1948).
110. *Chakrabarty*, 447 U.S. at 305, 310.
111. *Id.* at 309–10.
112. *Myriad*, 133 S. Ct. at 2117.
113. *Id.*
114. *Funk Bros. Seed Co.*, 333 U.S. at 132.
115. *Id.* at 128–30.
116. *Id.* at 130, 132.
117. *Id.* at 131.

would occur independently of any effort by Myriad, the isolated DNA was patent-ineligible subject matter.[118] Therefore, considering *Chakrabarty* and *Funk Brothers*, the Court concluded that the cDNA, but not the isolated DNA, constituted patent-eligible subject matter.[119]

C. *Guidance from the U.S. Patent and Trademark Office*

Following *Mayo*, the U.S. Patent and Trademark Office ("USPTO") issued a memorandum ("the First Memorandum") that set forth a *Mayo*-centered prong for patent application examiners to use in determining subject matter eligibility.[120] If the examiner is unable to identify "additional elements/steps or a combination of elements/steps," then the claim is not patent-eligible subject matter, and the application will be rejected.[121] For example, because the Court determined that Prometheus's patent merely sought "to apply the [natural] laws in question," its patent would be rejected by the USPTO under the First Memorandum's guidelines.[122]

Following *Myriad*, the USPTO issued another memorandum ("the Second Memorandum") directing examiners to reject composition claims that are based only on naturally occurring nucleic acids or fragments of naturally occurring nucleic acids, regardless of whether the nucleic acids are isolated.[123] However, this memorandum expressly stated that claims relating to non-naturally occurring nucleic acids, such as cDNA or a nucleic acid in which the order of the naturally occurring nucleotides has been altered, remain patent eligible under § 101.[124] The memorandum pointedly addressed the patent eligibility of nucleic acids, without addressing the effect of *Myriad* on other biotechnology claims.[125] As a result, drafters and litigators were left to blindly guess whether biotechnology claims outside of nucleic acid subject matter pass § 101 muster.

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118. *See Myriad*, 133 S. Ct. at 2117 (citing 35 U.S.C. § 101 (2012)) ("Myriad found the location of the BRCA1 and BRCA2 genes, but that discovery, by itself, does not render the BRCA genes 'new . . . composition[s] of matter,' § 101, that are patent eligible.").

119. *Id.* at 2116–19.

120. Memorandum from Deputy Commissioner for Patent Examining Policy Andrew H. Hirshfeld for Patent Examining Corps (July 3, 2012), *available at* http://www.uspto.gov/patents/law/exam/2012_interim_guidance.pdf.

121. *Id.* at 2.

122. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1299 (2012).

123. Memorandum from Deputy Commissioner for Patent Examining Policy Andrew H. Hirshfeld for Patent Examining Corps (June 13, 2013), *available at* http://www.uspto.gov/patents/law/exam/myriad_20130613.pdf.

124. *Id.*

125. *Id.*

Then, in March of 2014, the USPTO released its most recent memorandum entitled "2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting Or Involving Laws of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products" ("the Third Memorandum").[126] It sought to address changes in the law following *Myriad* and *Mayo*.[127] It explicitly superseded the Second Memorandum[128] and provided a series of six factors weighing in favor of eligibility and six factors weighing against eligibility for examiners to consider.[129] The examiner is directed to conduct a "factor-based analysis" and "[i]f the totality of the relevant factors weighs against eligibility, the claim should be rejected" as "not significantly different" from the underlying law of nature.[130]

While there may appear to be value in the flexibility afforded by twelve specifically demarcated factors to consider, there is also hidden hazard. A multitude of factors drastically increases the discretion afforded to the examiner, makes later review of the decision more time consuming, and arguably lessens the definiteness of the examination process as a whole. Moreover, in several of the hypothetical product and method claims provided to illustrate application of the multifactorial test, the memorandum simply states that the claim fails to satisfy certain factors without explaining *why* it fails.[131] Therefore, aside from bullet pointing new considerations, the Third Memorandum fails to clarify the analytical process for practitioners.

III. THE TRIANGLE METHOD: A PROPOSED GUIDE FOR BIOTECHNOLOGY PATENT CLAIMS AND § 101 PATENT-ELIGIBLE SUBJECT MATTER

Based on the recent line of Supreme Court cases, I propose a Triangle Method to strengthen biotechnology patent claims in the face of § 101 challenges. The Triangle Method achieves the results sought by the USPTO memoranda and the relevant case law but

126. Memorandum from Deputy Commissioner for Patent Examining Policy Andrew H. Hirshfeld for Patent Examining Corps (Mar. 4, 2014), *available at* http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf.

127. *Id.* at 1.

128. However, the memorandum also expressly stated that it is not intended to affect analysis of abstract ideas. *Id.*

129. *Id.* at 4–5.

130. *Id.* at 4.

131. For example, Example B summarily concludes the composition is not eligible subject matter "because the claim as a whole does not recite something significantly different from the natural product, e.g., because the claim does not include elements . . . that add significantly more . . . and also does not include features that demonstrate that the recited product is markedly different from what exists in nature." *Id.* at 7. This rationale provides little to no practical guidance for practitioners moving forward.

with improved clarity and greater efficiency. The three-part framework provides valuable prefiling guidance for inventors, drafters, and litigators so that claims may be situated in the most defendable position at an early stage in the patent's life cycle.

A. Side One: Inventiveness

The first side of the Triangle Method requires satisfaction of the "inventiveness" requirement articulated in *Mayo*. Application of the *Mayo* inventiveness condition requires two steps.[132] First, it must be determined whether the method claim at issue is directed to or comprises a law of nature, a natural phenomenon, or an abstract idea.[133] If the first step is answered in the affirmative, the second step asks whether the remaining aspects of the claim, once the underlying law of nature is discounted, encompass additional features that go beyond "well-understood, routine, conventional activity previously engaged in by scientists who work in the field."[134]

With *Mayo*'s two-step inquiry in mind, claims should clearly articulate elements or steps, or combinations therein, that are sufficiently larger than the natural principle either recognized or incorporated in the patent.[135] Moreover, the claims should show that the natural principle is being applied in both a new and practical manner never before seen in the field. These new steps must be inextricably combined with the claimed methods or compositions in order to combat an allegation that the claim simply states the natural law and directs the user to "apply it."

Indeed, in *Mayo*, the claimed processes would have been patentable if they had provided new steps for the practical application of metabolite-effectiveness correlation, instead of merely claiming the correlation's very existence.[136] Some believe that if Prometheus had recited a particular process for determining the level of metabolite in the blood, the claim would have likely survived.[137] Therefore, the key to satisfying the first side of the triangle is for drafters to establish and litigators to highlight an

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132. George R. McGuire & Blaine T. Bettinger, *How the Supreme Court Got It Right in* Mayo v. Prometheus, 10 SCITECH LAW. 12, 13 (2013).

133. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1293 (2012); McGuire & Bettinger, *supra* note 132.

134. *Mayo*, 132 S. Ct. at 1298.

135. This "inventiveness" requirement has not been restricted to medical diagnostic processes. *See, e.g.*, Alice Corp. Pty. v. CLS Bank Int'l, No. 13-298, slip op. at 1 (U.S. June 19, 2014) (holding that computer system method claims were not patent-eligible subject matter in light of *Mayo*'s inventiveness requirement).

136. *See Mayo*, 132 S. Ct. at 1297–98 ("[A] process reciting a law of nature [is not patentable] unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself.").

137. McGuire & Bettinger, *supra* note 132, at 15.

"inventive" quality that goes beyond the qualities of the subject matter as it is found in nature in as many clearly articulable ways as possible.

B. Side Two: Structural Differences

After *Myriad*, mere isolation of naturally occurring genes and genetic material does not constitute a structural alteration. Claim 1 in Myriad's patent only addressed the genetic information in the isolated DNA and did not address "the specific chemical composition of a particular molecule."[138] This recitation was to Myriad's detriment. The cited genetic information was identical to the genetic information as it is found in nature.[139] Therefore, the isolated DNA was ineligible for patent protection.[140]

This language and reasoning suggest that structural changes, if sufficiently prominent, would satisfy § 101 requirements. Justice Thomas explained for the majority that "[s]cientific alteration of the genetic code presents a different inquiry" than the inquiry in *Myriad* and hinted that "DNA in which the order of the naturally occurring nucleotides has been altered" may constitute patent-eligible subject matter.[141] As such, the structural changes are key.

Using this same line of structure-based analysis, the Court determined the man-made cDNA to be patent-eligible subject matter.[142] Even though the "nucleotide sequence of cDNA is dictated by nature, . . . the lab technician unquestionably creates something new when cDNA is made" because portions of the naturally occurring sequence are extricated while other portions are left unaltered.[143] However, the dispositive weight of such structural changes is dependent on the circumstances. Indeed, Justice Thomas stated that a "very short series of DNA may have no intervening introns to remove when creating cDNA. In that situation, a short strand of cDNA may be indistinguishable from natural DNA."[144]

Therefore, in order to steer away from the unpatentable subject matter appearing in Myriad's Claim 1, and more toward the patentable subject matter appearing in Myriad's Claim 2, drafters and litigators should emphasize the presence and quality of structural differences between the claimed composition and the naturally occurring subject matter. Practitioners should carefully illustrate that the structural changes constitute "the creation of a

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138. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2118 (2013); *see also* '282 Patent, *supra* note 93, at col. 153 l. 56–58.

139. *Myriad*, 133 S. Ct. at 2118; *see also* '282 Patent, *supra* note 93, at col. 153 l. 56–58.

140. *Myriad*, 133 S. Ct. at 2118.

141. *Id.* at 2120.

142. *Id.* at 2119.

143. *Id.*

144. *Id.*

unique molecule" that is "not . . . chemically identical," but instead wholly "invented."[145]

C. *Side Three: Informational or Functional Differences*

The Triangle Method's third side encompasses both informational and functional characteristics. This combination avoids unduly restricting the method's application to those biotechnology inventions that have clear "informational" characteristics such as the genetic information contained in DNA.

In *Myriad*, the Court explained that the unpatentable claims erroneously focused solely on the isolated DNA's genetic information, which was identical to the genetic information in the naturally occurring DNA.[146] However, this aspect of the holding does not invalidate all claims focusing on a given biotechnology's informational and functional characteristics. Claim 1 was unpatentable subject matter because it was completely devoid of any informational or functional *differences*.[147] The isolated DNA had identical genetic information to the DNA found in its naturally occurring state, and thus its function—to code for the BRCA mutation—was identical as well.[148] The inferential premise is that informational or functional differences between a claimed composition and naturally occurring subject matter, if sufficiently stark, may constitute a "new and useful . . . composition of matter" eligible for patent protection.

This conclusion is evidenced, in part, by the Court determining Myriad's cDNA claims to be patent-eligible subject matter.[149] Myriad removed codes for all other naturally occurring genetic components in creating the cDNA.[150] The natural DNA's information, and thus its function, was thereby significantly altered. This informational and functional alteration sufficiently differentiated the claimed cDNA from naturally occurring DNA.[151] Thus, the Court held that the cDNA in Claim 2 was patent-eligible subject matter.[152]

Therefore, to fortify biotechnology patent claims against § 101 challenges, any reference to functional or informational components of the claimed composition or process should be accompanied by an explanation that plainly differentiates the claimed function or

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145. *Id.* at 2118.

146. *Id.* at 2116, 2118.

147. *Id.* at 2116; '282 Patent, *supra* note 93, at col. 153 l. 56–58.

148. *Myriad*, 133 S. Ct. at 2113 ("Put differently, claim 1 asserts a patent claim on the DNA code that tells a cell to produce the string of BRCA1 amino acids."); *see also* '282 Patent, *supra* note 93, at col. 153 l. 56–58.

149. *Myriad*, 133 S. Ct. at 2119.

150. *Id.*; *see also* '282 Patent, *supra* note 93, at col. 49 l. 15 to col. 52 l. 27 (describing the process of identifying cDNA for the BRCA gene).

151. *Myriad*, 133 S. Ct. at 2119.

152. *Id.*

information from the naturally occurring function or information. In conjunction with the other two sides of the Triangle Method, this spotlighting will position the invention as more akin to the cDNA with its clear functional differences and less akin to the DNA with its functional similitude.

IV. APPLICATION OF THE TRIANGLE METHOD TO STAP CELLS

To illustrate the Triangle Method's practical application, I have analyzed the STAP cells discussed in Part I under each of the triangle's sides. The STAP cell creation method and the STAP cells themselves may be considered patent-eligible subject matter if the proper characteristics are emphasized in the patent's claims.

A. STAP Cells and Side One: Inventiveness

As to the first side of the Triangle Method—inventiveness, which encompasses the two-step *Mayo* framework—the creation of STAP cells is seemingly directed to or comprising a law of nature or natural phenomenon.[153] Under the first *Mayo* step, the natural phenomenon is the innate ability of adult multipotent cells to achieve pluripotent characteristics.[154] Coauthor of the STAP cell papers, Dr. Charles Vacanti, explained that the research team's primary goal was "to shed light on . . . a previously unrecognized biologic phenomenon that causes mature cells to revert to stem cells."[155] The team believes this process "is exactly what happens in the body during attempts to repair any damaged or diseased tissue."[156] So, in essence, the team "attempted to mimic the environment of injured tissues."[157] As a result, if the focus is to remain on "Mother Nature's way of responding to injury,"[158] the creation of STAP cells may "simply describe . . . natural relations."[159] Under this characterization, the process is simply a recitation of a natural phenomenon.

Applying the second step in the *Mayo* analysis, the underlying law of nature must be discounted to determine whether the invention adds an inventive component or step that goes beyond "well-understood, routine, conventional activity" common in

153. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1293 (2012) (discussing the first step in the analysis).

154. *Vacanti Interview*, *supra* note 37.

155. *Id.*

156. *Id.*

157. *Id.*

158. Ian Sample, *Simple Way to Make Stem Cells in Half an Hour Hailed as Major Discovery*, THEGUARDIAN (Jan. 29, 2014, 12:07 PM), http://www.theguardian.com/science/2014/jan/29/make-stem-cells-major-discovery-acid-technique.

159. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1297 (2012).

industry practice.[160] It could be argued that because the creation of STAP cells is so straightforward, it fails to add the necessary inventive quality for patent eligibility. Dr. Vacanti explained that the process is straightforward and without "subtleties."[161] Ricardo Dolmetsch, the Global Head of Neuroscience at Novartis Institutes for Biomedical Research, explained that "[f]rom a practical point of view . . . this will make the processes of making stem cells a lot simpler and a lot easier to scale."[162] Chris Mason, a professor of regenerative medicine bioprocessing at University College London asked, "How much easier can it possibly get[?]"[163]

Nevertheless, "ease" is not the decisive factor for patent-eligible subject matter and it cannot be said that STAP cell creation is so "well known" in the industry that there is no "inventive concept" in the application of the process.[164] Indeed, the "obviousness" of a claimed process is to be analyzed under § 103, not § 101.[165] While the creation of STAP cells may seem obvious "once known," hindsight is 20-20.[166] To avoid these potential hang-ups, the inventiveness side of the Triangle Method directs practitioners to highlight that no "scientist engaged in" an attempt to invoke an adult cell's pluripotent capabilities "would likely have utilized a similar approach."[167]

Before the inventors' papers were published, the application of external forces to create pluripotent stem cells was not used in the field.[168] Obokata and her team were the first to try and confirm the STAP cell–creation process.[169] Myriad, on the other hand, "was not the first to map a BRCA gene to its chromosomal location"[170] and

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160. *Id.* at 1292.

161. *Vacanti Interview*, *supra* note 37.

162. Maan Pamintuan-Lamorena, *New Advances in Stem Cell Research Could Become a Game Changer*, JAPAN DAILY PRESS (Jan. 30, 2014), http://japandailypress.com/new-advances-in-stem-cell-research-could-become-a-game-changer-3043305/.

163. Morin, *supra* note 28.

164. *Mayo*, 132 S. Ct. at 1299.

165. The Court in *Mayo* expressly warned not to conflate the two analytical sections; to do so would render "the 'law of nature' exception to § 101 patentability a dead letter." *Id.* at 1303.

166. *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2119–20 (2013) (explaining that a claimed process is patent ineligible where it is "already in use, or purely conventional").

167. Ass'n for Molecular Pathology v. USPTO, 702 F. Supp. 2d 181, 202–03 (S.D.N.Y. 2010), *aff'd in part, rev'd in part*, 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

168. *Researchers Create Embryonic Stem Cells Without Embryo*, *supra* note 22.

169. *Id.*

170. *Ass'n for Molecular Pathology*, 689 F.3d at 1348 (Bryson, J., concurring in part, dissenting in part).

"did not invent a new method of nucleotide sequencing."[171] Focusing on the innovative qualities of the process, it can hardly be disputed that the creation of STAP cells goes beyond previous cellular reprogramming techniques.

To combat potential challenges, the STAP cell–method claims must focus on the specific, controlled, and "inventive" work of the scientists as a necessary component for systematically reverting adult stem cells into a pluripotent state. It must be shown that the claimed method goes beyond the reversion process as it occasionally occurs in nature. Indeed, as stated in paragraph 236 of the U.S. patent application title page, the researchers' process reveals that pluripotency occurs "when cells are transiently exposed to strong stimuli that they would not normally experience in their living environments."[172] Therefore, side one of the Triangle Method dictates this inventive quality be underscored.

B. STAP Cells and Side Two: Structural Differences

Looking to side two of the Triangle Method, which addresses structural differences, it must be clearly demonstrated that STAP cells are not merely isolated compositions that remain identical to stem cells as they are found in nature.[173] Obokata explained, "It was really surprising to see that such a remarkable transformation could be triggered simply by stimuli from outside of the cell."[174] While the distinction may be elusive upon first glance, Obokata's statement suggests that the STAP cells' internal structure is not altered by humans in any capacity. In fact, the STAP cells' selling trait seems to be that they have no marked difference from the structural characteristics of naturally occurring pluripotent stem cells.[175]

However, the Triangle Method's structural side compels an emphasis on STAP cells as "the result of human intervention into nature," requiring "transformative steps" by the lab technician.[176] It should be stressed that STAP cells are not a result of "merely isolating the products of nature by extracting them from their natural location and making those alterations that are attendant to their extraction."[177] The STAP cells are not extracted in their whole

171. *Id.* at 1349.

172. '631 Patent Application, *supra* note 33, at 68.

173. *Id.* at 46 (claiming "[a] composition comprising a pluripotent cell, wherein the pluripotent cell is generated from a cell by the methods" in the preceding claims).

174. Morin, *supra* note 28.

175. *See* '631 Patent Application, *supra* note 33, at 13 (explaining that the claimed method produces pluripotent cells without "requir[ing] introduction of foreign reprogramming actors").

176. *Ass'n for Molecular Pathology*, 689 F.3d at 1329.

177. *Id.* at 1350.

and unaltered state.[178] Dr. Vacanti explained that the research team was "making these cells rather than isolating them."[179] He goes on to say, "[i]t may be a subtle, but we feel very important difference."[180] In fact, the two papers describe the process as a "reprogramming" of the cells.[181]

Therefore, the focus must remain on the STAP cell as wholly changed from its natural state, thereby "unquestionably creat[ing] something new."[182] For example, Claims 42, 43, and 44 in the patent application refer to "the removal of a portion of the cytoplasm" that simultaneously removes a certain percentage of the mitochondria from the cytoplasm.[183] Focusing on these structural alterations, Obokata's crafted STAP cells are distinguishable from Myriad's merely isolated DNA because the STAP cells constitute "the creation of a unique molecule" that is "not . . . chemically identical," but instead entirely "invented."[184]

C. STAP Cells and Side Three: Informational or Functional Differences

At first blush, the informational characteristics of the STAP cells are precisely the characteristics possessed by naturally occurring pluripotent stem cells, suggesting patent-ineligible subject matter. For example, Claim 31 in the patent application claims a method "wherein the epigenetic state of the cell is altered to more closely resemble the epigenetic state of an embryonic stem cell."[185] The express goal is to achieve a high degree of similarity in informational characteristics.[186]

As explained in Part II, Myriad's isolated DNA claim was patent-ineligible subject matter because it was devoid of any informational differences.[187] On the other hand, Myriad's man-made cDNA claim was patent eligible because Myriad removed codes for all other naturally occurring genetic components, thereby

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178. *Vacanti Interview*, *supra* note 37.

179. *Id.*

180. *Id.*

181. Obokata et al., *Bidirectional Developmental Potential*, *supra* note 22, at 679; Obokata et al., *Stimulus-Triggered Fate Conversion*, *supra* note 22, at 641; *see also Vacanti Interview*, *supra* note 37 (discussing the "reprogramming" of cells).

182. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2119 (2013).

183. '631 Patent Application, *supra* note 33, at 45–46.

184. *Myriad*, 133 S. Ct. at 2118 (internal quotation marks omitted).

185. U.S. Patent Application No. 61/779,533, at 74 (filed Mar. 13, 2013), *available at* http://patentscope.wipo.int/search/docservicepdf_pct/id00000022881386.pdf.

186. *See id.* at 25 (discussing the selection of cells "displaying the desired characteristics" and "exhibiting pluripotency").

187. *See supra* notes 101–05 and accompanying text.

altering the cDNA's original genetic information in the process.[188] In light of the Court's distinction between the DNA and cDNA, the third side of the Triangle Method directs practitioners to highlight any informational and functional alterations.[189]

To do so, STAP cells should be strictly characterized as adult stem cells with pluripotent capabilities. A naturally occurring adult stem cell's "functional portion" is based on its multipotent capabilities, whereas a STAP cell's "functional portion" is based on its reverted pluripotent capabilities. Pluripotency is found in naturally occurring *embryonic* stem cells, not naturally occurring *adult* stem cells.[190] Therefore, adult STAP cells are unlike any adult stem cell found in nature.

Paragraph 214 of the patent application explains that "STAP cells may represent a new metastable pluripotent state closely related to but distinct from that of [embryonic stem] cells."[191] Yet, the "distinct from" aspect is not adequately highlighted in either the title page or the claims. Even the language in paragraph 211, which seeks to set forth possible differences between STAP cells and embryonic cells as observed in mice, indicates only that they are "partially distinct."[192] Without an articulable explanation of these differences, challengers and courts could easily focus on the similarities between STAP cells and naturally occurring embryonic cells instead of the innovative differences.

CONCLUSION

Innovation in the biotechnology industry is quickly exceeding the boundaries of the current patent law system, specifically with regard to § 101 patent-eligible subject matter. Thomas Jefferson did not anticipate personalized diagnostic bench-top systems or customized organ transplants at the Patent Act's conception.[193] Likewise, Congress and the Judiciary cannot anticipate the medical advancements in years to come. However, drafters and litigators can take steps today to protect biotechnology patent claims against possible challenges. To do so, the statutory framework and recent

188. *See supra* notes 106–09 and accompanying text.

189. For example, in *Diamond v. Chakrabarty*, the Court held that the claimed bacteria composition was patent-eligible subject matter largely because it possessed *functional* characteristics that differed from naturally occurring bacteria and therefore provided significant value in oil spill treatment. 447 U.S. 303, 305, 310 (1980).

190. PETERS, *supra* note 22.

191. '533 Patent Application, *supra* note 185, at 62.

192. *Id.*

193. *See* Rick Weiss, *How Do You Patent a New Elephant?*, WASH. POST, Sept. 20, 1987, at C3 (explaining that "Thomas Jefferson[] didn't have much to say about monoclonal antibodies" or various other twenty-first century biotechnology advancements).

legal reasoning must be united both comprehensively and practicably.

The Triangle Method provides a flexible approach that incorporates recent Supreme Court reasoning to ensure a claim is more easily defendable in the face of § 101 challenges. The three sides may be adapted to the particulars of the biotechnology at issue. Practitioners may rely more heavily on one side than another in order to fortify the weaknesses of a given claim. For example, where the informational or functional differences are not particularly pertinent to an invention, adequately articulated structural differences may nevertheless cast the claims as patent eligible. To be sure, Myriad's claim for the isolated DNA failed to address any structural differences and instead only addressed informational characteristics.[194] It was deemed unpatentable subject matter as a result. Thus, the Triangle Method mandates that all three sides be addressed in some capacity to lay the foundation for a sound validity defense.

The Triangle Method addresses the biotechnology characteristics deemed most important and persuasive by the Supreme Court in *Mayo* and *Myriad*. It also comports with the approach articulated in the most recent USPTO memorandum to reach the same outcome in a more simplistic and efficient manner. Moreover, the Triangle Method recognizes that inventors often build upon foundational scientific concepts as they are found in nature. Indeed, "all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious."[195] As biotechnology patents thrive and scientific research flourishes, practitioners need clear guidance in shaping their work to fit the contours of the current patent-eligible subject matter legal landscape.

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194. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2118 (2013); *see also* U.S. Patent No. 5,837,492 (filed Apr. 29, 1996), *available at* http://patft.uspto.gov/netahtml/PTO/srchnum.htm (query "5837492"); '282 Patent, *supra* note 93; U.S. Patent No. 5,693,473 (filed Jun. 7, 1995), *available at* http://patft.uspto.gov/netahtml/PTO/srchnum.htm (query "5693473").

195. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1304 (2012) (quoting Diamond v. Diehr, 450 U.S. 175, 189 n.12 (1981)) (internal quotations omitted).

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