STEMMING THE TIDE: ON THE PATENTABILITY OF STEM CELLS AND DIFFERENTIATION PROCESSES

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Embryonic stem cells present novel questions of patentable subject matter eligibility. This Note examines the patentability of two types of patents: embryonic stem cells and methods of differentiating embryonic stem cells. After explaining patentable subject matter doctrine and ways of testing whether an invention is patentable, the Note posits that neither type of invention is patentable because the biological principles involved in both types of inventions are almost identical to the biological phenomena that occur naturally in the developing embryo. Additionally, the Note explains that, from a normative standpoint, patents should not be granted over these inventions.

INTRODUCTION

Embryonic stem cells will change our lives. Scientists as well as the media proclaim that these cells may soon be used in therapies reminiscent of science fiction: replacing organs, reversing paralysis for accident victims, or rejuvenating the heart following a heart attack. Indeed, these possibilities may become realities within our lifetimes. However, it would be troubling if only a few corporations exclusively control these therapies, which may become the case if certain types of patents are allowed. One important question is who, if anyone, owns intellectual property rights to these therapies? This Note posits that neither embryonic stem cells nor the methods of differentiating these cells in the laboratory are patentable subject matter because they are almost identical to the cells and processes that occur naturally in the developing embryo. Additionally, this Note explains why these patents are undesirable from a policy perspective.

This Note is the first to address the patentability of methods of differentiating embryonic stem cells into different cell types. Because differentiation is the key to making embryonic stem cells therapeutically useful, patents over such processes may prove extremely valuable and claim the keys for achieving the potential of stem cell–based

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therapies. This Note also provides insight into the patent eligibility of embryonic stem cells themselves, a subject that has received limited attention in the literature.

This inquiry into the patentable subject matter eligibility of embryonic stem cells and differentiation processes is timely given the recent surge in academic and judicial interest in patentability following the Supreme Court's decisions in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*[1] and *Bilski v. Kappos*.[2] This increased interest is especially noticeable in regard to the patentability of life science inventions and medical procedures. For example, the Federal Circuit recently decided *Association for Molecular Pathology v. U.S. Patent & Trademark Office* (*Myriad*),[3] which reversed a district court's holding that DNA sequences are not patentable subject matter. A petition for certiorari has since been filed with the Supreme Court.[4] And most recently, on March 20, 2012, the Supreme Court decided *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*,[5] holding that the relationship between concentrations of metobolites in the blood and likely patient responsiveness to a drug regimen is not patentable. While there has not yet been any litigation regarding stem cell patents, such litigation is very likely since stem cell–based therapies will eventually reach the market and, like prescription drugs, will involve multiple players in competition for patent rights.

This Note uses scientific publications in support of its arguments regarding patentable subject matter. For example, it applies scientific literature to show that differentiation method patents use the same compounds that cause natural differentiation in the developing embryo. This approach is unusual because "[a]s a general matter, lawyers and science don't mix."[6] That is, lawyers and judges untrained in science may miss some of the finer nuances in arguments regarding scientific principles, a fact that Judge Learned Hand famously

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[1] 548 U.S. 124, 125, 134 (2006) (Breyer, J., dissenting) (discussing the patentability of the correlation between vitamin deficiency and disease).

[2] 130 S. Ct. 3218, 3231 (2010) (discussing the patentability of a mathematical formula for hedging in the commodities and energies markets); *see also* Symposium, *The Future of Patents:* Bilski *and Beyond*, 63 STAN. L. REV. 1245 (2011) (discussing the implications of *Bilski* and related emerging patent law issues).

[3] 653 F.3d 1329 (Fed. Cir. 2011), *petition for cert. filed sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 11-725 (U.S. Dec. 7, 2011).

[4] Petition for a Writ of Certiorari, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 11-725 (U.S. Dec. 7, 2011). This is a new direction for the Supreme Court which "ha[d] not recently considered the patentability of products derived from nature." Michael Risch, *Everything Is Patentable*, 75 TENN. L. REV. 591, 612 (2008).

[5] No. 10-1150 (U.S. Mar. 20, 2012).

[6] *See* Peter Lee, *Patent Law and the Two Cultures*, 120 YALE L.J. 2, 4 (2010).

lamented.[7] This Note endeavors to fill this gap by integrating legal and scientific frameworks.

The Note proceeds in three Parts. Part I begins by discussing the patent system in general and patentable subject matter doctrine in particular. It lays out current doctrinal tests for determining whether a given invention qualifies for a patent. Part II introduces embryonic stem cells and their potential therapeutic uses as well as the two types of patents that are the focus of this Note—patents on stem cells and patents on differentiation methods. Part III applies the doctrinal tests for patentable subject matter to these patents and ultimately concludes that, because of the scientific facts involved in each, neither qualifies for patent protection. Finally, Part III also discusses normative arguments against granting such patents.

I
PATENTABLE SUBJECT MATTER

Patents are government-granted rights to exclusively control inventions. Patent rights are administered by the United States Patent and Trademark Office (USPTO).[8] These rights of exclusivity can be very valuable because they prohibit anyone else from making, using, selling, or offering to sell, either directly or indirectly, the patented invention.[9] Parties that infringe these rights may be found liable for monetary damages in civil suits.[10]

Patents are not automatically handed out to the first to file a patent application. Rather, they are granted only following a review process known as an examination, which is performed by one of the

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[7] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 115 (S.D.N.Y. 1911) ("I cannot stop without calling attention to the extraordinary condition of the law which makes it possible for a man without any knowledge of even the rudiments of chemistry to pass upon such questions as these. The inordinate expense of time is the least of the resulting evils . . . ."), *aff'd in part, rev'd in part*, 196 F. 496 (2d Cir. 1912).

[8] *See generally The USPTO: Who We Are*, U.S. PATENT & TRADEMARK OFFICE, http://www.uspto.gov/about/index.jsp (last visited Mar. 20, 2012). The Constitution grants Congress the power to establish a patent system. U.S. CONST. art. I, § 8, cl. 8 ("The Congress shall have Power . . . To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries . . . ."). Congress has exercised this power by enacting the Patent Act of 1952. Pub. L. 82-593, 66 Stat. 792 (1952). Patent law is based on the statutes and the courts' interpretations of them.

[9] 35 U.S.C. § 271(a)–(c) (2006). These rights last for twenty years from the time of filing. *Id.* § 154(a)(2).

[10] *Id.* § 281. Damages can be very high, as in the $1.67 billion judgment against Abbott Laboratories for infringing its competitor's patent. *Abbott Loses Drug Patent Suit*, N.Y. TIMES, June 30, 2009, at B2.

USPTO's more than 6200 examiners.[11] A patent is granted unless the examiner is able to meet her burden of disproving that an invention is novel, is nonobvious, has utility, and provides an adequate disclosure of the invention.[12] The Patent Act states these requirements,[13] which are meant to ensure that patents are granted only in furtherance of the "useful Arts."[14] An overarching requirement, in addition to the above, is that an invention must fit within the scope of patentable subject matter that Congress laid out in 35 U.S.C. § 101, as interpreted by the courts.[15] This Note concerns this last requirement, and the next Subpart describes the judicially constructed tests that may be used to determine whether an invention meets the patentable subject matter requirement.[16]

A. Categorical Exclusions from Patentability

Section 101 of the Patent Act lists four categories of patentable subject matter: "any new and useful process, machine, manufacture, or composition of matter."[17] In keeping with the term "any," the categories in this section have historically been viewed broadly.[18] In fact,

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[11] U.S. PATENT & TRADEMARK OFFICE, PERFORMANCE AND ACCOUNTABILITY REPORT FISCAL YEAR 2010, at 153 (2010) (providing personnel statistics from 2006–10). On average, this process takes approximately twenty-six months. *Id.* at 61.

[12] This reverse burden reflects the presumption of patentability. *See, e.g.*, U.S. PATENT & TRADEMARK OFFICE, U.S. DEPT. OF COMMERCE, MANUAL OF PATENT EXAMINING PROCEDURE § 2163.04 (8th ed. 2010) (explaining that "[t]he examiner has the initial burden" to disprove that the written description requirement has been met).

[13] *See* 35 U.S.C. §§ 101, 102, 103, 112 (detailing novelty, nonobviousness, utility, and disclosure requirements).

[14] U.S. CONST. art. 1, § 8, cl. 8. These requirements "are meant to ensure that the average benefits from disclosure and innovative effort stimulated by patents are greater than the average social costs—including administrative costs—that patents generate." John M. Golden, *Patentable Subject Matter and Institutional Choice*, 89 TEX. L. REV. 1041, 1055 (2011).

[15] While the requirement that an invention relate to patentable subject matter may be considered at the same time or even after the other requirements discussed above, this Note treats § 101 as having a gatekeeping role, which makes the inquiry a threshold question. *See* Eileen M. Kane, *Patent Ineligibility: Maintaining a Scientific Public Domain*, 80 ST. JOHN'S L. REV. 519, 519 (2006) (referring to § 101 as a gatekeeper). Treating the patentable subject matter requirement as an initial inquiry disentangles it from the other requirements and focuses the discussion on § 101.

[16] Due to the complexity of the patentable subject matter inquiry and lack of clear rules in regard to its adjudication, an early treatise on patent law described it as "a very difficult branch of the law of patents." WILLARD PHILLIPS, THE LAW OF PATENTS FOR INVENTIONS 73 (Boston, Am. Stationers' Co. 1837). I therefore enter this discussion with slow and careful steps.

[17] 35 U.S.C. § 101.

[18] *See, e.g.*, Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980) ("In choosing such expansive terms . . . modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope.").

the Supreme Court has quoted the Patent Act's legislative history to say that "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'"[19] Nonetheless, these categories do have limits.

For instance, there are three judicially created exclusions to patentability that apply even when an invention fits one of the categories of § 101. Namely, "laws of nature, physical phenomena, and abstract ideas" are not patentable.[20] Professor Duffy writes that the Court has attempted to justify these exceptions with textualist statutory interpretation but has also acknowledged that these exceptions have been in place since the mid-1800s and are not required by the statutory text.[21] In order to understand patentable subject matter, it is necessary to examine these three exceptions and see how courts determine whether an invention fits within them. The three exceptions are somewhat intertwined, so for the purposes of my analysis I will address physical phenomena together with laws of nature before engaging in a separate discussion of abstract ideas.

1. Physical Phenomena and Laws of Nature

The physical phenomena exception encompasses things that occur naturally. *O'Reilly v. Morse*,[22] a Supreme Court decision from 1853, illustrates this concept.[23] The case involved Morse's patent over

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[19] *Id.* at 309 (quoting S. REP. NO. 82-1979, at 5 (1952)). For criticism arguing that this statement has been taken out of context and that Congress intended to retain the traditional requirements of patentability, which may not have allowed patents over living things, see Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 373–74 (2002).

[20] Bilski v. Kappos, 130 S. Ct. 3218, 3225 (2010) (quoting *Chakrabarty*, 447 U.S. at 309) (internal quotation marks omitted).

[21] John F. Duffy, *Why Business Method Patents?*, 63 STAN. L. REV. 1247, 1274 (2011) ("The Justices in the [*Bilski*] majority finally felt the need to justify the judge-made exceptions to patentability, and they did so by bringing (or by attempting to bring) the exceptions into the framework of textualism."). Many have been critical of the use of these exceptions. *See, e.g.*, Aaron J. Zakem, Note, *Rethinking Patentable Subject Matter: Are Statutory Categories Useful?*, 30 CARDOZO L. REV. 2983 (2009) (criticizing the categorical approach to patentable subject matter because it is both over- and underinclusive). One critic, Justice Frankfurter, remarked that categorical exceptions "only confuse[ ] the issue" because they are "vague and malleable terms." Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 134–35 (1948) (Frankfurter, J., concurring). Suggestions for improvement include codifying the exceptions to patentability so that they will be more clear and predictable. *E.g.*, Kane, *supra* note 15, at 556 (proposing changes).

[22] 56 U.S. (15 How.) 62 (1853).

[23] Another case illustrating this concept was *Le Roy v. Tatham*, in which a patent for making lead pipes was at issue. 55 U.S. (14 How.) 156 (1852). The *Le Roy* Court held that "[a] principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as no one can claim in either of them an exclusive right." *Id.* at 175. The case described electricity and "any other power in nature" as such phenomena. *Id.*

the telegraph. Specifically, the Court reviewed whether Morse could patent the principle of transmitting characters through an electric wire—the *idea* of the telegraph.[24] Morse's patent did not seek to limit the use of the principle to any specific field or machine and acknowledged that anyone using this phenomenon would be an infringer were the patent to be found valid.[25] The Court held that such a principle encompassing a physical phenomenon could not be patented because it would preclude "the onward march of science": Its broad scope would simply "shut[ ] the door against inventions of other persons" because it prevented anyone from using electric signals to transmit messages.[26]

According to some writers, the physical phenomena category closely tracks other patentability requirements such as novelty, non-obviousness, and utility.[27] Others suggest that the idea underlying this exclusion, as well as the other exclusions, is the need to allow science to expand and "to keep the basic means of scientific research available"—that is, the raw material on which scientists experiment—because this is the only way truly to "promote the Progress of Science and useful Arts" as the Constitution requires.[28]

A similar analysis determines whether a patent claim falls under the exclusion against laws of nature. For example, in the famous 1948 *Funk Bros.* case, the inventor "discovered that there are strains of each species of root-nodule bacteria which do not exert a mutually inhibitive effect on each other."[29] This was quite an important discovery at the time because until then bacteria had to be sold by individual strain to farmers who wanted to help their plants fix nitrogen; it was commonly believed that bacterial strains could not be mixed because of inter-strain inhibitory effects. The Court, however, said that this discovery was not patentable because "[i]t is not more than the discovery of some of the handiwork of nature."[30] The reason for excluding laws of nature from patentability, as explained by the *Funk*

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[24] *O'Reilly*, 56 U.S. (15 How.) at 112–13.

[25] *Id*. at 112 (quoting the patent's author as stating, "I do not propose to limit myself to the specific machinery or parts of machinery described in the foregoing specification and claims").

[26] *Id.* at 113.

[27] *E.g.*, Emir Aly Crowne-Mohammed, *Can You Patent That? A Review of Subject Matter Eligibility in Canada and the United States*, 23 TEMP. INT'L & COMP. L.J. 269, 274–75 (2009).

[28] Stephen Pessagno, Prometheus *and* Bilski*: Pushing the Bounds of Patentable Subject Matter in Medical Diagnostic Techniques with the Machine-or-Transformation Test*, 36 AM. J.L. & MED. 619, 624 (2010) (quoting U.S. CONST. art. I, § 8, cl. 8) (internal quotation marks omitted).

[29] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

[30] *Id.* at 131.

Bros. Court, was similar to the physical phenomena exception: "[Q]ualities of . . . bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are . . . reserved exclusively to none."[31] The principle is clear: If something occurs naturally, one may not own a patent over it, and mankind may continue improving upon it. Professor Kane explains that this categorical exclusion also includes "the genetic code that defines the relationship between DNA and protein" or any "fundamental scientific relationship[ ]" between several variables.[32]

2. Abstract Ideas

The final category of exclusion––abstract ideas––includes algorithms, formulas, and mental steps.[33] When a claimed invention can be reduced to one of these, it is not patent eligible. For instance, in *Gottschalk v. Benson*, the Court held that an algorithm for converting binary-coded decimal numerals into pure binary numerals was not patentable because it was an abstract idea.[34] The Court took notice of the fact that a patent on the conversion method would in essence prevent anyone else from using the algorithm, holding that allowing the patent "would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself."[35]

For similar reasons, the invention in *Parker v. Flook* could not receive a patent. *Flook* centered on a claimed "Method for Updating Alarm Limits" that employed a mathematical formula in order to gauge the optimal operating conditions of a catalytic conversion process.[36] Unlike in *Benson*, the *Flook* method did not cover every potential use, but the claims were still not patentable because "once that algorithm [was] assumed to be within the prior art, the

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[31] *Id.* at 130.

[32] Kane, *supra* note 15, at 552–53.

[33] *See, e.g.*, Parker v. Flook, 437 U.S. 584, 585–86 (1978) (disallowing a patent over a method for updating alarm limits in an industrial process); Gottschalk v. Benson, 409 U.S. 63, 64–67 (1972) (describing the respondent's application to patent an algorithm for converting numerical computer coding). For an explanation of the mental steps exclusion, see *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124, 129–30 (2006), in which the claimed method involved mentally determining a therapeutic dosage.

[34] 409 U.S. 63 (1972). For additional discussion of this case, see Pessagno, *supra* note 28, at 626–27. Even though this decision is from 1972, it is one of only a few recent decisions regarding patentable subject matter, as this is a topic that the Supreme Court has not addressed for the past thirty years.

[35] *Benson*, 409 U.S. at 72; *see also* Clara R. Cottrell, *Most Valuable Patent: The Use of Natural Phenomena in Patents*, 7 WAKE FOREST INTELL. PROP. L.J. 251, 266–67 (2007) (discussing the *Benson* Court's reasoning).

[36] *Flook*, 437 U.S. at 585–86.

application, considered as a whole, contain[ed] no patentable invention."[37] That is, assuming that a formula or algorithm is already in existence, one must discover more than the formula itself in order to receive patent protection, and furthermore, any such discovery must be more than insignificant post-solution steps.[38]

Most recently, *Bilski v. Kappos* dealt with inventors who filed a patent application claiming a series of steps explaining how to use hedging, a system for protecting against risk.[39] They described this concept through a mathematical formula and claimed a method of using it specifically in the commodities and energy markets.[40] Rejecting their claims as unpatentable subject matter, the Supreme Court held that the invention was merely an abstract idea and could not be patented even if limited to those specific markets.[41] The Court found that allowing these claims "would effectively grant a monopoly over" hedging because it "would pre-empt use of this approach in all fields," a concept over which no one may claim a property right.[42]

The overarching concern in the case of abstract ideas involves the fear that overbroad claims take something fundamental away from society. As Professor Lemley suggests, by looking at the breadth of claims and analyzing whether they "encroach[ ] upon society's right to unfettered access to scientific truths," courts can reach an equilibrium between the incentive-granting and the public knowledge–expanding goals of the patent system.[43]

B. Doctrinal Tests for Patentability

In addition to the preceding description of the three categorical exceptions, legal scholarship and case law suggest two basic tests to summarize the exceptions to patentability. First, patents are not granted for inventions that may preempt ideas already in "the storehouse of knowledge of all men," including basic tools of science or abstract ideas.[44] In this vein, the Court recently mentioned preemp-

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[37] *Id.* at 594.

[38] *See id.* (describing the patentability of post-solution steps and discussing why the application of the respondent's formula is not patentable).

[39] 130 S. Ct. 3218, 3231 (2010).

[40] *Id.*

[41] *Id.*

[42] *Id.*

[43] Mark A. Lemley et al., *Life After* Bilski, 63 STAN. L. REV. 1315, 1329 (2011).

[44] *Bilski*, 130 S. Ct. at 3225 (quoting Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948)) (internal quotation marks omitted). For an overview of preemption, see generally Rochelle C. Dreyfuss & James P. Evans, *From* Bilski *Back to* Benson*: Preemption, Inventing Around, and the Case of Genetics Diagnostics*, 63 STAN. L. REV. 1349, 1353–61 (2011).

tion of further inventions as a reason for denying patents.[45] Second, patents are only granted for truly "inventive" inventions that produce something different from what occurs naturally. As explained below, lower courts may not be applying this inventiveness test explicitly, but I argue that the test is evident in the Court's patentable subject matter jurisprudence. Overall, while neither test is statutorily required nor universally recognized, courts and scholars rely on some version of preemption or inventiveness to make sense of § 101.

1. The Preemption Test

The preemption test investigates whether a patent could prohibit anyone else from employing a fundamental principle that would be beneficial for society to utilize. According to Professors Dreyfuss and Evans, the preemption test is justified by the fact that fundamental principles are very difficult to "invent around"—to create an invention that does not incorporate the principles.[46] Disallowing preemptive patents is justified because the cost of granting exclusivity over such basic ideas outweighs the potential benefits of such exclusivity.[47] This concern explains the results of *Bilski*, *Benson*, and *O'Reilly*, described above, where the Court found no patentable subject matter because it determined that a patent in those cases would have prevented, respectively, the use of hedging, the binary-conversion algorithm, and electricity to transmit characters. These processes were so broad and fundamental that there was no way to invent around the claims at issue in those cases. The Court did not believe that anyone should have exclusive control over these naturally occurring ideas.[48]

Preemption also has underlaid the Court's upholding of patents in several instances. In *Diamond v. Diehr*, the patent claimed the use of a well-known mathematical formula in a process for curing synthetic rubber.[49] Even though this formula, which by itself would be

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[45] *See* Dreyfuss & Evans, *supra* note 44, at 1351 ("The [*Bilski*] Justices . . . agree[d] on one thing: a patent that 'preempts' something . . . is very bad indeed. 'Preempt' is used in each of the *Bilski* opinions.").

[46] *See id.* at 1352 (explaining the inability to invent around as an important factor in preemption).

[47] For more on these social costs, and for a mathematical model illustrating the need to perform a preemption analysis in order to achieve an optimal result with patents, see generally Golden, *supra* note 14, at 1055, 1067–74.

[48] Bryan Treglia argues that the preemption test is not a good measure "because it does not account for scope." Bryan Treglia, *Patentable Subject Matter: Separating Abstract Ideas and Laws of Nature from Patentable Inventions*, 48 JURIMETRICS J. 427, 437 (2008). He maintains that the preemption test—or any other test of patentable subject matter—should account for the range of an invention's applications because those with narrow applications do not prevent other new inventions. *Id.*

[49] 450 U.S. 175, 187 (1981).

considered an abstract idea, was present in the claims, the invention was still found patent eligible because the patentees did "not seek to pre-empt the use of that equation. Rather, they [sought] only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process."[50] In other words, preemption concerns are abated when a patent claims only a very specific application of a law of nature accompanied by additional conditions; the patent propertizes only that specific application, instead of the whole equation. Such claims "may well be deserving of patent protection."[51]

2. *The Inventiveness Test*

Another test for patentable subject matter looks at the "inventive" characteristic of the patent claims: It allows patents for claims that include an actual invention or use of creativity rather than a recitation of naturally occurring ideas. As one scholar explains, without an additional invention on top of a scientific insight, "there simply would be no discovery *of an inventor*."[52] Before explaining the details of this test, two things should be noted: First, the concept is a relatively avant garde way of looking at patentability. It has not been explored extensively in legal scholarship, but as Professors Sarnoff, Demaine, and Fellmeth explain, it has a long-standing precedential

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[50] *Id.* at 187. In *Flook*, the claims to a formula for setting alarm limits were written in a way that limited them to the petrochemical industry so that they did not actually prevent the use of the formula in other applications. In contrast with *Diehr*, however, this did not allow for patenting because such limitations were deemed "post-solution activity." Parker v. Flook, 437 U.S. 584, 590 (1978). This seems to tie the preemption and inventiveness ideas together: Post-solution activities do little to ameliorate preemption concerns and do not add any inventive step to the patent. Inventiveness is outlined in greater detail in Subpart I.B.2.

[51] *Diehr*, 450 U.S. at 187. An example of this principle is found in the *Telephone Cases*, where, similar to *O'Reilly*, the patent claimed a specific way of using electricity to transmit sounds. 126 U.S. 1, 531 (1888). The Court upheld the patent in the *Telephone Cases* because it covered only one method for electrical sound transmission and did not preempt other methods. *Id.* at 534–35. The Court added, "It may be that electricity cannot be used at all for the transmission of speech except in the way Bell has discovered . . . but that does not make his claim one for the use of electricity distinct from the particular [patented] process." *Id.* at 535. The Court thereby emphasized that the proper inquiry in preemption is whether a patent preempts the use of a natural phenomenon.

[52] Joshua D. Sarnoff, *Patent Eligible Inventions After* Bilski 20 (Feb. 7, 2011) (unpublished manuscript), *available at* http://ssrn.com/abstract=1757272. This idea is tied to Professor Sarnoff's discussion of God as an inventor and the need for humanity to share natural scientific *discoveries*—as opposed to human inventions. *See id.* at 40–48 ("[T]he divine origins of discoveries of nature . . . imposed moral duties to freely share knowledge of science, nature, and ideas.").

grounding.[53] Second, the inventiveness test is especially important to consider when dealing with purified products of nature, including embryonic stem cells, which are in a sense purified from the cells in a developing embryo.[54] Some lower courts have found purified products to be patentable,[55] but the Supreme Court has never adopted this view—in fact, it goes against the Court's earlier precedent: Without an inventive aspect, mere purification inventions cannot lead to patentability.[56]

One way to examine claims for inventiveness is to ask whether they produce something that is markedly different from a naturally occurring phenomenon or idea.[57] As Chief Justice Marshall once explained,

> It is not every change of form and proportion which is declared to be no discovery, but that which is simply a change of form or proportion, and nothing more. If, by changing the form and proportion, a new effect is produced, there is not simply a change of form and proportion, but a change of principle also.[58]

The late nineteenth-century Supreme Court put this in terms of "change in the manner of application [or] result substantially distinct in its nature."[59] While this may sound like an argument about an

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[53] *See generally id.* (explaining the historical background of the inventiveness test). For an overview of this requirement, situating it among other requirements of patentability, see generally Demaine & Fellmeth, *supra* note 19, at 330–60. *See also* Brief of Amici Curiae the Am. Coll. of Med. Genetics et al. in Support of Petitioners at 20–26, Mayo Collaborative Servs. v. Prometheus Labs., Inc., No. 10-1150 (U.S.), 2011 WL 4071917, at *20–26 [hereinafter College of Medical Genetics Brief] (discussing inventiveness); Brief of Nine Law Professors as Amici Curiae in Support of Petitioners at 4–20, *Prometheus*, No. 10-1150 (U.S.), 2011 WL 4071921, at *4–20 (same).

[54] For an explanation of the biology underlying stem cells, see *infra* notes 95–99 and accompanying text.

[55] *E.g.*, Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (S.D.N.Y. 1911), *aff'd in part, rev'd in part*, 196 F. 496 (2d Cir. 1912). *Parke-Davis* is distinguishable from patentable subject matter cases because it did not examine the validity of the asserted patent. Rather, it looked at novelty. For a discussion of the applicability of this and other old cases in the patentability inquiry, see Robin Feldman, *Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law*, 63 STAN. L. REV. 1377, 1396–98 (2011).

[56] *See* Am. Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593 (1874) (requiring purification to involve significant alteration in order to be patent eligible); *see also* Demaine & Fellmeth, *supra* note 19, at 339 (discussing lower court decisions following *American Wood-Paper* that denied patents to purified products with only an increase in therapeutic benefits).

[57] For more on the markedly different standard, see *infra* notes 63–64 and accompanying text.

[58] Davis v. Palmer, 7 F. Cas. 154, 159 (C.C. Va. 1827) (No. 3645) (Marshall, C.J.).

[59] Ansonia Brass & Copper Co. v. Elec. Supply Co., 144 U.S. 11, 18 (1891) (quoting Pa. Ry. v. Locomotive Safety Truck Co., 110 U.S. 490, 494 (1883)). Arguably this was a case

invention's novelty,[60] the question of patentable subject matter is distinct from the novelty inquiry as it is not concerned with what is "prior art" under 35 U.S.C. § 102, but rather asks if the invention by itself is patentable regardless of what prior art exists.[61]

The Court's nineteenth-century thinking, requiring a change in "form and proportion" that also changes "effect" or "principle," has endured through the twentieth century and into the twenty-first. For example, in *Funk Bros.*, in which the Supreme Court invalidated a bacteria-mixture patent because the interaction of the two species was simply a naturally occurring phenomenon, the patentee had done nothing to make the resulting product any different than it was in nature.[62] In essence, the realization that the two species do not inhibit each other was merely a discovery of scientific insight and therefore not patent eligible. Contrast *Funk Bros.*, however, with the 1980 case of *Diamond v. Chakrabarty*, where the Court allowed a patent claiming a genetically engineered bacterium because it had properties "possessed by no naturally occurring bacteria."[63] Chakrabarty inserted into the bacteria two plasmids coding for enzymes involved in hydrocarbon degradation, which would allow it singlehandedly to clean up oil spills—something that no other species of microorganism could do. In this way, the inventor "produced a new bacterium with *markedly different* characteristics from any found in nature,"[64] which meant he could receive a patent.

Despite the initial appearance of being based on precedent, at least in terms of the "markedly different" language, *Chakrabarty* was an unexpected decision to many in the field. As Professor Duffy explains in detail, the practice before *Chakrabarty* was to allow patents only over inanimate inventions and not over living things.[65] This may have been attributable to the fact that in pre-biotechnology days, plants were the only living things that could be substantially manipulated to create distinct new varieties, and plant varieties were pro-

about novelty, but patentable subject matter was deeply intertwined with novelty and nonobviousness prior to the 1952 Patent Act.

[60] Some argue that the idea of an invention being markedly different from what is found naturally can be better understood in terms of novelty or nonobviousness. *See, e.g.*, Zakem, *supra* note 21, at 3009–11 (suggesting using these other patent provisions).

[61] *See also infra* note 80 (providing the Court's response to a similar argument on interrelatedness of novelty and patentable subject matter).

[62] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948); *see also supra* notes 29–31 and accompanying text (discussing *Funk Bros.*).

[63] 447 U.S. 303, 305 (1980).

[64] *Id.* at 310 (emphasis added).

[65] *See* John F. Duffy, *Rules and Standards on the Forefront of Patentability*, 51 WM. & MARY L. REV. 609, 625–29 (2009).

tected by the Plant Patent Act.[66] But this changed when, through progress in biotechnology, humans obtained the tools to create living things that nature itself does not make. For example, Chakrabarty's role in the invention of his claimed bacteria (inserting two plasmids) could not be attributed to nature, but rather to mankind. Also, as Duffy notes, biotechnology allowed inventors to adequately describe the full process of making their products for the first time, whereas "[b]reeders of new plants or animals could not explain through any written description how to recreate those living things."[67] Thus, *Chakrabarty*'s "markedly different" language seems geared towards a distinction between inventions of nature and inventions to which humankind made a significant contribution.[68]

Today, this "markedly different" language continues to hold sway. This past summer, the Federal Circuit[69] used this test to declare that genetic sequences are patentable. In *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, also known as the *Myriad* case, the Federal Circuit faced an appeal from a district court's ruling that Myriad Genetics' patents for the BRCA genes are directed to nonpatentable subject matter.[70] The appellate court reversed the district court's decision because, as one of the three opinions explained,[71] the claimed isolated genetic sequences are "markedly different—[that is,] have a distinctive chemical identity and

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[66] *Id.* at 626–27. The Plant Patent Act was enacted in 1930. Pub. L. No. 245, 46 Stat. 376 (codified as amended at 35 U.S.C. §§ 161–164 (2006)).

[67] Duffy, *supra* note 65, at 630. Duffy states another weakness of a per se rule against patenting living inventions: It could be circumvented by claiming the living invention together with an inanimate carrier material, for example by claiming a bacteria on top of a petri dish. *Id.* at 631–32.

[68] *See* Christopher M. Holman, Bilski*: Assessing the Impact of a Newly Invigorated Patent-Eligibility Doctrine on the Pharmaceutical Industry and the Future of Personalized Medicine* 4 (June 23, 2009) (unpublished manuscript), *available at* http://ssrn.com/abstract=1424493 ("[T]he key distinction is human intervention; products and processes arising out of active human invention are patent-eligible . . . .").

[69] The use of one nationwide appeals court, the Court of Appeals for the Federal Circuit, is unique to patent litigation. The Federal Circuit was founded pursuant to the Federal Courts Improvement Act of 1982. Pub. L. No. 97-164, 96 Stat. 25 (codified in scattered sections of 28 U.S.C.); *see also History of the Court*, FED. CIR. HIST. SOC'Y, http://www.federalcircuithistoricalsociety.org/historyofcourt.html (last visited Mar. 20, 2012) (providing a general overview of the Federal Circuit). The Federal Circuit's jurisdiction covers appeals for cases arising under the patent laws, decisions of the United States Court of Federal Claims, and some civil suits brought against the United States. 28 U.S.C. § 1295 (2006).

[70] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 653 F.3d 1329 (Fed. Cir. 2011), *petition for cert. filed sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 11-725 (U.S. Dec. 7, 2011). Commentators refer to this case as *Myriad* because Myriad Genetics, Inc. is the assignee of the patents at issue.

[71] For a discussion of the three opinions from the circuit court and their applicability to the stem cell field, see *infra* notes 136–46 and accompanying text.

nature—from molecules that exist in nature" due to the addition of new chemical bonds to the DNA molecule.[72] Even though the same genetic sequences for BRCA and its mutations exist naturally in the human body, the actual isolated strands of DNA do not;[73] they must be removed from their environment in the cell and manipulated chemically in order to be isolated.[74] According to the Federal Circuit, this makes such isolated sequences patentable subject matter.[75]

Yet it is not clear whether this is the same analysis of markedly different that the *Chakrabarty* Court contemplated. Chemical bonds are a somewhat arbitrary metric for determining differences because, in the case of DNA, they do not give a unique meaning to the claimed polynucleotide, which still codes for the same gene and can have the same breast cancer susceptibility mutation that is the essence of the invention in *Myriad*. Also, if the Supreme Court intended chemistry alone to suffice for marked difference, it would have found the combination of bacteria in *Funk Bros.* to be patentable because of the chemical interaction of the inhibitory molecules secreted by the different bacteria.[76] Therefore, it is not clear that chemical differences should always be taken as indicators of whether an invention is markedly different for inventiveness purposes.[77]

Given the ambiguities surrounding the markedly different standard, it should be noted that there are other ways to conceptualize the inventiveness requirement. For example, inventiveness can also be assessed by looking at the "inventive faculty" that was used to create the invention.[78] One version of "inventive faculty" was explained in *Flook*, where the Court stated that the use of an abstract idea embodied in an algorithm or formula must be accompanied by other

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72 *Myriad*, 653 F.3d at 1351.

73 DNA is found in cells in long strands called chromosomes that have thousands of genes each. Therefore, isolated sequences coding for a single gene do not exist in nature.

74 *Myriad*, 653 F.3d at 1352.

75 As described in *supra* notes 55–56 and accompanying text, mere purification of a compound preexisting in nature does not make patentable subject matter, which explains why the *Myriad* opinions and oral argument focused on the differences between the isolated genetic material and genetic material found inside cells.

76 The sufficiency of chemistry alone also goes against the reasoning of the pre–Patent Act decision in *General Electric Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928). There, a patent over isolated tungsten was held invalid even though tungsten is only found in nature chemically bound to other atoms and possesses very different characteristics when isolated. *Id.* at 642–43.

77 The second *Myriad* opinion in favor of patentability focused on the difference in utility, which is also not in line with patentable subject matter jurisprudence. *See infra* notes 142–46 and accompanying text.

78 College of Medical Genetics Brief, *supra* note 53, at 8 (quoting Dann v. Johnston, 425 U.S. 219, 225 (1976)) (internal quotation marks omitted).

meaningful steps in order to ensure patentability.[79] Post-solution or merely data-gathering steps are not inventive enough to receive patent protections, so a claim must add more than such steps to any algorithm it employs.[80] Similarly, limiting an abstract idea's application to a particular field is not enough by itself for patentability, as in *Bilski*, which tried to limit hedging to energy markets.[81]

Despite criticism from some scholars who believe that the analysis in *Flook* was wholly overruled in *Diehr*,[82] the Court did not do this when it wrote that "claims must be considered as a whole" and that "[i]t is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis."[83] Rather, the Court was discussing dissection of claims for purposes of determining novelty and obviousness, matters which are dealt with by other sections of the Patent Act, namely 35 U.S.C. §§ 102 and 103, respectively.[84] Emphasizing this point, the *Diehr*

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[79] Parker v. Flook, 437 U.S. 584, 594–96 (1978); *see also supra* notes 37–38 and accompanying text (discussing *Flook*).

[80] The *Flook* Court explained this in another useful way citing older Supreme Court patent cases: The algorithm element of the claim should be "treated as though it were a familiar part of the prior art," thereby requiring that there be a novel contribution somewhere else in the patent in order to grant patent protection to the invention. *Flook*, 437 U.S. at 591–92. Responding to the argument that this mixes the novelty and nonobviousness analyses of 35 U.S.C. §§ 102 and 103 with the patentable subject matter inquiry, the Court said that this requirement necessarily falls under § 101 because (1) it ensures that skilled patent claims draftsmen would be unable to circumvent the subject matter requirement by adding additional steps to an algorithm and (2) it clarifies the requirement that a patent contain an actual invention. *Flook*, 437 U.S. at 592–94. A similar view has taken hold in the international context as the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) also contains an invention requirement. *See* Emir Aly Crowne Mohammed, *What Is an Invention? A Review of the Literature on Patentable Subject Matter*, 15 RICH. J.L. & TECH. ¶ 31 (2008), http://law.richmond.edu/jolt/v15il/article2.pdf ("TRIPS arguably creates a subject matter threshold . . . in that there must first be an 'invention.'").

[81] Bilski v. Kappos, 130 S. Ct. 3218, 3230 (2010) ("[T]he prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula to a particular technological environment' or adding 'insignificant postsolution activity.'" (quoting Diamond v. Diehr, 450 U.S. 175, 191–92 (1981))).

[82] *See, e.g.*, Mark A. Lemley, *Point of Novelty*, 105 NW. L. REV. 1253, 1278–79 (2011) (arguing that the analysis in *Flook* has been overruled). Lemley discusses the applicability of the "point of novelty" test to different areas of patent law. He criticizes using the idea in patentable subject matter because "[u]nder that approach, many drugs would be unpatentable because the discovery of their efficacy is merely identification of a previously unknown natural phenomenon. Computer software would be unpatentable, since it is composed of algorithms." *Id.* at 1278. For the opposite view, see Sarnoff, *supra* note 52, at 30–31, which describes the importance of the inventiveness requirement and problems with the Court's decision in *Diehr*.

[83] *Diehr*, 450 U.S. at 188.

[84] *See id.* at 191 (referring to the inquiry above as relating to novelty and nonobviousness). A similar contrast between inventiveness and nonobviousness is made in Demaine & Fellmeth, *supra* note 19, at 365–84.

Court repeated *Flook*'s idea that post-solution steps do not contribute to patentability.[85] And, in *Bilski*, after reaffirming its rule against post-solution activity from *Flook*, the Court also stated that "[t]he [*Flook* patent] application's only *innovation* was reliance on a mathematical algorithm," thereby highlighting the need for inventiveness.[86] Therefore, *Flook*, *Diehr*, and *Bilski* all seem to imply that inventiveness may be an important factor in determining patentability.

While the preemption and inventiveness tests are the most appropriate ways to view the question of patentable subject matter, some scholars who are critical of these tests have suggested other ways to frame the inquiry. Professor Lemley, for example, suggests looking broadly at the scope of a claim and balancing factors that focus not only on the claims but also on the industry and technological field.[87] Taking a more philosophical approach, Ariel Simon recommends making the comparison to "provisional tools for answering questions that we have about the world around us" and preventing the patenting of such claims.[88] Regardless of which test is used, the cases discussed here indicate that certain inventions cannot be granted patents on various grounds that are broadly related to the fundamental statutory categories of patentable subject matter. The following Part discusses implications for the biotechnology industry.

II
Patentable Subject Matter, the Biotechnology Industry, and Stem Cells

The patentable subject matter analysis is very important to biotechnology innovation. Many potentially patentable biotechnology inventions involve cells or their components, or knowledge gained from studying naturally occurring processes in living organisms. Given current doctrine, such traits make these inventions possible candidates

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[85] *Diehr*, 450 U.S. at 191–92.

[86] *Bilski*, 130 S. Ct. at 3230 (emphasis added); *see also* Pamela Samuelson & Jason Schultz, *"Clues" for Determining Whether Business and Service Innovations Are Unpatentable Abstract Ideas*, 15 Lewis & Clark L. Rev. 109, 114–15 (2011) (arguing that *Bilski* "reaffirmed as sound precedent" the set of clues to unpatentability in *Flook*).

[87] *See* Lemley et al., *supra* note 43, at 1341 (suggesting factors for determining patentability).

[88] Ariel Simon, *Reinventing Discovery: Patent Law's Characterization of and Interventions upon Science*, 157 U. Pa. L. Rev. 2175, 2200–01 (2009). The Federal Circuit has also tried this approach in the case of abstract ideas, determining patentability solely by use of the machine or transformation test, which would grant a patent if a claim is tied to a machine or transforms matter. *E.g.*, *In re* Bilski, 545 F.3d 943, 954 (Fed. Cir. 2008). But the Supreme Court declined to uphold this test as a standalone measure of patentability. Bilski v. Kappos, 130 S. Ct. 3218, 3231 (2010).

for exclusion from patentability. And while there is a healthy debate about both the right to patent any biotechnology inventions and about the importance of patents in promoting innovations,[89] there can be little doubt that patent protection plays a major role in the growth and innovation of the biotechnology industry.[90] The industry claims that it needs patent protection because innovation in the field has a high risk of failure and patents are a way to attract and assure those investors who are willing to put capital into risky endeavors.[91] These arguments are equally pertinent to biotechnology's young subfield of stem cell research, which is introduced in this Part. Following an introduction to the basics of stem cell science and terminology, this Part provides an overview of patents that have been issued over stem cell–related inventions, which are the main focus of this Note.

A. Human Embryonic Stem Cells

The term "stem cell" is quite old[92] but is generally used to refer to a cell that is able to self-renew and produce non-stem daughter cells through cell division.[93] Stem cells are found in various parts of our

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[89] *See infra* Part III.C (discussing policy issues). *See generally* VANDANA SHIVA, BIOPIRACY: THE PLUNDER OF NATURE AND KNOWLEDGE (1997) (stating grounds for opposing any property right over living things).

[90] For a discussion of the subject, see generally GRAHAM DUTFIELD, INTELLECTUAL PROPERTY RIGHTS AND THE LIFE SCIENCE INDUSTRIES 191–211 (2009). *See also* J. Adam Holbrook, *Are Intellectual Property Rights Quanta of Innovation?*, *in* THE ROLE OF INTELLECTUAL PROPERTY RIGHTS IN BIOTECHNOLOGY INNOVATION 26, 26 fig.1.1 (David Castle ed., 2009) (illustrating the flow of ideas and money in biotechnology).

[91] *See* DUTFIELD, *supra* note 90, at 193 ("Biotechnology was and continues to be a high risk and extremely research intensive activity, and for dedicated biotechnology firms especially, it has always been crucial to be able to secure large amounts of investment capital . . . . Patent portfolios . . . are a magnet for outside investors . . . ."). Highlighting the importance of patents to the biotechnology industry, the Biotechnology Industry Organization (BIO), an industry group representing over 1200 biotechnology companies, lobbies for patent legislation and policy making that is favorable to the industry. *See, e.g.*, Letter from James C. Greenwood, President & CEO, Biotechnology Indus. Org., to Mr. Kohlenberger and Ms. Farrell (May 25, 2010), *available at* http://www.bio.org/node/287 ("[P]atent incentives and flexible technology transfer policies and practices have propelled this nation to new heights in therapeutic development, agricultural efficiency, and environmental products."); *BIO Encourages Congress To Improve Patent System*, BIO.ORG (Mar. 3, 2009), http://www.bio.org/node/2025 ("The nation's strong patent system has enabled us to be a world leader on innovation.").

[92] Since originating in the mid-1800s, the term has had various uses. Miguel Ramalho-Santos & Holger Willenbring, *On the Origin of the Term "Stem Cell*," 1 CELL STEM CELL 35, 35 (2007).

[93] *E.g.*, NAT'L INSTS. OF HEALTH, U.S. DEPT. OF HEALTH & HUMAN SERVS., STEM CELL BASICS 1 (2009) [hereinafter STEM CELL BASICS], *available at* http://stemcells.nih.gov/staticresources/info/basics/SCprimer2009.pdf ("When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function."); Ramalho-Santos & Willenbring, *supra* note 92, at 35

bodies and are naturally utilized in healing injuries and in normal bodily functions. For example, hematopoietic stem cells continuously replace red and white blood cells, and skin stem cells are employed in regenerating broken skin.[94] These "adult" stem cells are different from embryonic stem cells, which have made headlines in recent years and are the subject of this Note. Here, I introduce the basic biology underlying embryonic stem cells and explain their therapeutic potential.

Human embryonic stem cells were first cultured[95] in 1998 by James Thomson at the University of Wisconsin.[96] Embryonic stem cells are derived from the inner cell mass of the pre-implantation blastocyst, a stage of human embryonic development occurring three to five days after fertilization.[97] These cells are unique in two important ways. First, embryonic stem cells are pluripotent—that is, they have the potential to become any cell type in the adult body.[98] Second, they are able to self-renew for extended periods of time in the laboratory,[99] which means that a single batch of stem cells can last a long time for laboratory research purposes.

Thanks to these unique properties, scientists hold high hopes for the use of embryonic stem cells in ways that can positively impact human lives. Most well known is the potential to use embryonic stem cells in cell replacement therapy. Such procedures could be useful for

("Stem cells are defined as having the capacity to both self-renew and give rise to differentiated cells.").

94 Robert Lanza & Nadia Rosenthal, *The Stem Cell Challenge*, SCI. AM., May 24, 2004, at 98. Other adult stem cell types include mesenchymal stem cells, neural stem cells, epithelial stem cells, and germ stem cells. *See* STEM CELL BASICS, *supra* note 93, at 10–11, 20.

95 In the biological sciences, to culture cells means to grow them in laboratory conditions. *Tissue Culture*, BIOLOGY ONLINE, http://www.biology-online.org/dictionary/Tissue_culture (last visited Mar. 20, 2012).

96 *See* James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCIENCE 1145 (1998). Scientists have used mouse embryonic stem cells since 1981. STEM CELL BASICS, *supra* note 93, at 2. For a general overview of embryonic stem cells, see Stacy Kincaid, *Oh, the Places You'll Go: The Implications of Current Patent Law on Embryonic Stem Cell Research*, 30 PEPP. L. REV. 553, 563–65 (2003).

97 Thomson et al., *supra* note 96, at 1145; STEM CELL BASICS, *supra* note 93, at 2. If left undisturbed and allowed to implant in the uterus, the blastocyst gives rise to a human fetus. Blastocysts used to create embryonic stem cells, however, are not taken from women but rather come from fertilized eggs left over after *in vitro* fertilization. *See* Nicholas Wade, *Grappling with the Ethics of Stem Cell Research*, N.Y. TIMES, July 24, 2001, at F3 ("The [embryos] are frozen in case of future need, but most have no realistic prospect of coming to term and will eventually be destroyed, an inevitable consequence of the fertility treatment.").

98 Joseph Itskovitz-Eldor et al., *Differentiation of Human Embryonic Stem Cells into Embryoid Bodies Comprising the Three Embryonic Germ Layers*, 6 MOLECULAR MED. 88, 93 (2000); Thomson et al., *supra* note 96, at 1145.

99 Thomson et al., *supra* note 96, at 1145; STEM CELL BASICS, *supra* note 93, at 3.

treating neurological diseases or injuries, including stroke, Parkinson's disease, and spinal cord trauma, where damaged or dead neural cells need to be replaced.[100] The range of potential therapies is great,[101] and some of the concepts involved have already been proven.[102] In fact, the first clinical trials are currently ongoing for the use of human embryonic stem cells in human subjects,[103] indicating that the science involved has reached a level that regulators believe shows real promise.

B. Differentiating Stem Cells

In order to realize these potential uses, embryonic stem cells must differentiate, or turn into specific cell types, a process made possible by their pluripotent characteristic.[104] Scientists are able to differentiate human embryonic stem cells into cardiomyocytes, pancreatic cells, and neural cells, among others,[105] which may then be used in cell

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[100] *See* Olle Lindvall, *Stem Cell Therapy for Human Neurodegenerative Disorders: How To Make It Work*, NATURE MED., July 2004, at S42 ("Transplantation of stem cells or their derivatives . . . have been proposed as future therapies for neurodegenerative diseases."). For a graduate student project highlighting such future prospects, see Leeron Morad, The Derivation of Neural Stem Cells and Potential Implications for Cell Replacement Therapy (2008) (unpublished M.S. thesis, University of California, Los Angeles) (on file with the Health Science Library, University of California, Los Angeles). For a discussion of techniques for using embryonic stem cells in stroke research, see Jin Zhong et al., *Hydrogel Matrix To Support Stem Cell Survival After Brain Transplantation in Stroke*, 24 NEUROREHABILITATION & NEURAL REPAIR 636 (2010).

[101] Cell replacement therapies for "burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis" are just some of the possibilities. STEM CELL BASICS, *supra* note 93, at 15.

[102] For example, proof of concept for Parkinson's disease therapies in a rat model has been shown. Dali Yang et al., *Human Embryonic Stem Cell–Derived Dopaminergic Neurons Reverse Functional Deficit in Parkinsonian Rats*, 26 STEM CELLS 55, 56–60, 62 (2008). Embryonic stem cells can also be used as *in vitro* models for diseases and drug screening. John McNeish, *Embryonic Stem Cells in Drug Discovery*, 3 NATURE REVS. 70, 75–79 (2004).

[103] Geron, a California-based company, initiated the first clinical trial in 2009. Stuart Fox, *FDA Approves First-Ever Stem Cell Clinical Trial*, POPULAR SCI. (Jan. 26, 2009, 10:56 A.M.), http://www.popsci.com/scitech/article/2009-01/fda-approves-first-ever-stem-cell-clinical-trial; Gretchen Vogel, *U.K. Approves Europe's First Embryonic Stem Cell Clinical Trial*, SCI. INSIDER (Sept. 22, 2011, 11:25 A.M.), http://news.sciencemag.org/scienceinsider/2011/09/uk-approves-europes-first-embryonic.html; *see also* Sue Dremann, *Paralyzed Bay Area Patient Gets Stem-Cell Therapy*, PALO ALTO ONLINE (Sept. 20, 2011, 11:01 A.M.), http://www.paloaltoonline.com/news/show_story.php?id=22594 (discussing the progress in the first U.S. clinical trial).

[104] *See generally* STEM CELL BASICS, *supra* note 93, at 7–8 (discussing the importance of differentiation and techniques that induce it); Morad, *supra* note 100, at 3 (same). Contrast differentiation with simply culturing the cells as defined in *supra* note 95, which involves growing the cells in laboratory conditions but does not necessarily imply any conversion process. Differentiation involves converting the cells into a different cell type.

[105] *E.g.*, Christine Mummery et al., *Differentiation of Human Embryonic Stem Cells to Cardiomyocytes: Role of Coculture with Visceral Endoderm-Like Cells*, 107 CIRCULATION

replacement therapy. Generally, directed differentiation, in which a culture of embryonic stem cells is caused to differentiate to a specific cell fate, is carried out by the addition or subtraction of growth factors and other components in the cells' culture medium.[106] Directed differentiation is important because if a patient needs to receive cardiomyocytes to help repair heart muscle tissue that has been damaged following a heart attack, it will not benefit the patient (or could even be lethal) to receive neural and skin cells in the therapeutic injection.

As previously explained, the biotechnology industry claims that it requires patent protection in order to foster growth and fund the development of new technologies. Because differentiation processes and certain types of cells are critical to any future embryonic stem cell–based therapies, it is not surprising that many patents have already been issued that cover various inventions in the stem cell field. Biotechnology companies have patented differentiation processes in addition to differentiated cells and embryonic stem cells themselves: It is estimated that there are over 250 patents related to embryonic stem cells.[107]

Considering the general societal discomfort surrounding individual ownership of products and inventions derived from the human body,[108] some debate about the patentability of these inventions is expected. What makes the debate even more interesting is that inventors outside of industry seek patent protection over stem cell–related inventions: Most of the issued patents in the field list academic

2733, 2733 (2003); J.H. Shim et al., *Directed Differentiation of Human Embryonic Stem Cells Towards a Pancreatic Cell Fate*, 50 DIABETOLOGIA 1228, 1229, 1235 (2007); Yang et al., *supra* note 102, at 60–61; Morad, *supra* note 100, at 4.

106 STEM CELL BASICS, *supra* note 93, at 7; *see also* Jaroslaw Czyz & Anna M. Wobus, *Embryonic Stem Cell Differentiation: The Role of Extracellular Factors*, 68 DIFFERENTIATION 167 (2001) (explaining the role of extracellular signaling molecules in differentiation); *infra* Part III.B (discussing differentiation patents and compounds used).

107 A search conducted on October 20, 2011 looked for "embryonic stem cell" in the title or abstract of issued patents and yielded over 250 results. *Patent Full Text Database Manual Search*, U.S. PATENT & TRADEMARK OFFICE, http://patft.uspto.gov/netahtml/PTO/search-adv.htm (last visited Mar. 20, 2012). Similarly, in 2001 there already were "191 patents with the term stem cell included in the abstract of the invention on its first page," Sabra Chartrand, *Patents: Amid the Debate on Stem Cell Studies, a Small but Growing Number of Patents Are Issued in the Field*, N.Y. TIMES, Aug. 13, 2001, at C2, whereas an equivalent of the 2001 search yielded 1548 patents in 2011.

108 *Cf.* Moore v. Regents of the Univ. of Cal., 793 P.2d 479, 489 (Cal. 1990) ("[The law] deal[s] with human biological materials as objects sui generis, regulating their disposition to achieve policy goals rather than abandoning them to the general law of personal property. It is these specialized statutes, not [property law], to which courts . . . look for guidance on the disposition of human biological materials.").

researchers as the inventors, a point this Note addresses in discussing incentives for patenting.[109]

C. Stem Cell Patents and the Patentable Subject Matter Question

In this Subpart, I introduce two categories of stem cell patents and discuss the biology underlying each one. Patents covering inventions in the stem cell field can be divided into two important categories: patents claiming embryonic stem cells themselves and patents for methods involving stem cells, such as methods of differentiating the cells. Other useful inventions in the field are not the subject of this Note because they do not appear to involve as intricate an analysis of patentable subject matter.[110]

The first category, covering the embryonic stem cells themselves, has a potentially very broad scope. These patents include, for example, claims over "[a] purified preparation of pluripotent human embryonic stem cells"[111] and "[a] replicating *in vitro* cell culture of human embryonic stem cells."[112] This is the only category that has received any treatment in the academic literature; authors have focused primarily on the Wisconsin Alumni Research Foundation (WARF) patents, namely U.S. Patent No. 6,200,806 and U.S. Patent No. 5,843,780.[113] At first glance, these patents appear to include in their scope *all* human embryonic stem cells. Media coverage has also latched onto this category in its coverage of the WARF patents.[114]

The focus on this category is for a good reason: Patents covering actual embryonic stem cells can be very broad and give wide owner-

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[109] *See infra* Part III.C (discussing policy issues relating to patentability).

[110] These may include methods of culturing embryonic stem cells. For more on this topic, see *infra* note 148 and accompanying text, explaining why culture methods should be patentable.

[111] U.S. Patent No. 6,200,806 col.21 ll.1–2 (filed June 26, 1998).

[112] U.S. Patent No. 7,029,913 col.21 ll.21–22 (filed Oct. 18, 2001); *see also* U.S. Patent No. 7,955,851 col.34 ll.6–8 (filed Sept. 21, 2009) (claiming "[a] cell culture comprising undifferentiated human pluripotent stem cells on an extracellular matrix in a culture medium").

[113] '806 Patent; U.S. Patent No. 5,843,780 (filed Jan. 18, 1996); *see, e.g.*, Christopher R. Carroll, *Selling the Stem Cell: The Licensing of the Stem Cell Patent and Possible Antitrust Consequences*, 2002 U. ILL. J.L. TECH. & POL'Y 435 (discussing antitrust issues related to the licensing of the '780 Patent); John A. Lee, *The Ownership and Patenting of Inventions Resulting from Stem Cell Research*, 43 SANTA CLARA L. REV. 597, 626–27 (2003) (explaining the ramifications of the '780 and '806 Patents on future embryonic stem cell research); Jenny Shum, Note, *Moral Disharmony: Human Embryonic Stem Cell Patent Laws, WARF, and Public Policy*, 33 B.C. INT'L & COMP. L. REV. 153, 161–62 (2010) (discussing the intersection between the WARF patents and U.S. policies that limit stem cell research funding). The '780 Patent is similar in its scope to the '806 Patent, but it was filed about two years before human embryonic stem cells were successfully cultured.

[114] *See, e.g.*, Sheryl G. Stolberg, *Patent on Human Stem Cell Puts U.S. Officials in Bind*, N.Y. TIMES, Aug. 17, 2001, at A1 (discussing policy implications of the WARF patents).

ship to a few entities. For example, claim 3 of the '806 Patent can be reasonably interpreted to encompass any human embryonic stem cells grown in laboratories because the claim simply describes normal human embryonic stem cells.[115] Thus, by asserting their exclusivity rights, WARF and other patentees and assignees who own similar patents can substantially impede research into embryonic stem cells by threatening researchers with lawsuits or demanding high royalties.

The second category of patents involves methods for differentiating embryonic stem cells into specific cell types. In order to be therapeutically viable, embryonic stem cells must undergo differentiation to become relatively homogenous populations of cells of a specific lineage so that they may be administered to a patient and repair a particular type of tissue. These patents claim methods of directed differentiation—to neural cells, hepatocytes, cardiomyocytes, as well as other cell lineages—through the culturing of embryonic stem cells in the presence of certain proteins or other factors that promote such differentiation.[116] Most of these patents call for exposing the embryonic stem cells to naturally occurring proteins in order to bring about the differentiation, though some call for using synthetic molecules to achieve this result. In fact, the only significant difference between the broadest claims in many of these method patents is the identity of the compound used to direct the differentiation.[117]

This second category is a more recent phenomenon than the first. It implicates discoveries that first required scientists to perfect methods for culturing embryonic stem cells and then entailed a great deal of trial and error in discovering which compounds affect differentiation. For this reason, the majority of inventions in this category have not yet been granted patents. Furthermore, this category is much

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[115] Claim 3 of the '806 Patent claims "[a] purified preparation of pluripotent human embryonic stem cells wherein the cells are negative for the SSEA-1 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have euploid karyotypes and in which none of the chromosomes are altered." '806 Patent col.21 ll.13–18. SSEA-1, SSEA-4, and alkaline phosphatase are markers used by scientists to determine whether they are working with pluripotent human embryonic stem cells, meaning that this claim covers exactly the cells scientists around the world use in their research. *See* Lee, *supra* note 113, at 626 ("All human embryonic stem cell research in the United States falls under the [WARF patents] . . . . ").

[116] *E.g.*, Directed Differentiation Method for Making Cardiomyocytes from Human Embryonic Stem Cells, U.S. Patent No. 7,452,718 (filed Mar. 21, 2005); U.S. Patent No. 7,332,336 (filed Feb. 27, 2004) (method for differentiation into hepatocytes); Hematopoietic Differentiation of Human Embryonic Stem Cells, U.S. Patent No. 6,613,568 (filed Aug. 27, 2001); Making Neural Cells for Human Therapy or Drug Screening from Human Embryonic Stem Cells, U.S. Patent No. 6,833,269 (filed May 31, 2001).

[117] *Compare* '269 Patent (method for neural differentiation though the addition of neutrophins), *with* U.S. Patent No. 7,772,001 (filed Jan. 3, 2006) (method for endodermal differentiation through the addition of hepatocyte growth factor).

larger than the first because there are many more ways to differentiate cells than to claim the embryonic stem cells themselves. The category is expected to continue expanding as stem cell research progresses.

Most of the current literature on these patents—focusing on the WARF patents—inquires into moral issues surrounding stem cell patents and raises questions about patenting human beings and the right to use embryos in patented technologies.[118] Other scholars focus on policy-oriented issues such as the role of patents in promoting innovation in biotechnology and stem cell research through the exclusivity incentive they present.[119] Some attention has been given to the question of whether embryonic stem cells represent patentable subject matter,[120] yet the analysis in the literature has been short, disconnected from the science, and has not been updated to incorporate recent jurisprudence on patentability. Importantly, the patentable subject matter implications for differentiation processes have gone unnoticed. The next Part carries out this analysis.

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[118] For a comprehensive overview of the ethical principles involved in all sides of the debate, including religious, business, and medical ethics, see generally Samuel Packer, *Embryonic Stem Cells, Intellectual Property, and Patents: Ethical Concerns*, 37 HOFSTRA L. REV. 487 (2008). *See also* LI WESTERLUND, LIFE SCIENCE INVENTIONS 83–84 (2004) (explaining that ethical considerations are important given their relevance to European patent law which considers morality when determining patentability); Gregory R. Hagen & Sebastien A. Gittens, *Patenting Part-Human Chimeras, Transgenics, and Stem Cells for Transplantation in the United States, Canada, and Europe*, 14 RICH. J.L. & TECH. 11 (2008) (discussing broader morality concerns with biotechnology research and patents); Shum, *supra* note 113, at 159–60, 170–73 (discussing European concerns including the European Union's bar to patenting human embryos); Janice M. Mueller, *Patenting Human Embryonic Stem Cells in the United States: The Legal and Ethical Debate*, CASRIP NEWSLETTER (Ctr. for Advanced Study & Research on Intellectual Prop., Seattle, Wash.), Autumn 2007, at 1, *available at* http://www.law.washington.edu/Casrip/Newsletter/default.aspx?year=2007&article=newsv14i4StemCell (noting that embryonic stem cell research is controversial because the initial creation of the cells requires destroying an embryo). Since this Note does not discuss the morality issue, it does not further elaborate on the matter.

[119] *E.g.*, Michael S. Mireles, Jr., *States as Innovation System Laboratories: California, Patents, and Stem Cell Technology*, 28 CARDOZO L. REV. 1133 (2006) (looking at ways to incentivize research in the field); Julia W. Dovi, Comment, *Speaking Words of Wisdom: Let It Be The Reexamination of the Human Embryonic Stem Cell Patents*, 12 MARQ. INTELL. PROP. L. REV. 107, 118–25 (2008) (arguing that patents promote embryonic stem cell research progress); John Miller, Comment, *A Call to Legal Arms: Bringing Embryonic Stem Cell Therapies to Market*, 13 ALB. L.J. SCI. & TECH. 555, 568–75 (2003) (responding to arguments that patenting stem cells is desirable from a policy perspective).

[120] *E.g.*, Peter Yun-hyoung Lee, *Inverting the Logic of Scientific Discovery: Applying Common Law Patentable Subject Matter Doctrine To Constrain Patents on Biotechnology Research Tools*, 19 HARV. J.L. & TECH. 79, 104–05 (2005) (reaching inconclusive results on patentable subject matter); Miller, *supra* note 119, at 576–77 (supporting patentability); Russell Korobkin & Stephen R. Munzer, *Stem Cell Research and the Law* 49–55 (Univ. of Cal. L.A. Sch. of Law Research Paper No. 06-05, 2006), *available at* http://ssrn.com/abstract_id=878392 (same).

III
Stem Cells and Differentiation Process Patents: Legal and Policy Arguments Against Patentability

In this Part, based on the Supreme Court's interpretation of patentable subject matter principles and the underlying science, I argue that neither stem cells nor differentiation methods are patentable subject matter. In doing so, I explain how courts faced with these patentability questions should use the preemption and inventiveness tests to analyze the scientific differences between stem cell–based inventions and their naturally occurring equivalents in order to gauge whether they should receive patent protection. Finally, I apply normative ideas on patent incentives to buttress my conclusion regarding the patent ineligibility of these inventions.

A. The Patent Ineligibility of Embryonic Stem Cells

Stem cell inventions pose novel questions regarding patentable subject matter eligibility. This is partially due to our society's discomfort with individual ownership of products and inventions derived from the human body,[121] moral concerns, and the disconnect between science and law. Nonetheless, patents that claim actual stem cells fit comfortably within the § 101 "manufacture" or "composition of matter" categories. This is not a troublesome point, since the oil-metabolizing bacterium in *Chakrabarty* was treated as a manufacture.[122] Difficulty emerges, however, when the common law bars to patentability are considered. Do embryonic stem cells fall under any of the three exclusions: laws of nature, physical phenomena, or abstract ideas?

Embryonic stem cells do not fit easily into any of these three categories. On the one hand they are not similar to $E = mc^2$ or the law of gravity,[123] nor are they abstract like the hedging formula in *Bilski*.[124] On the other hand, embryonic stem cells may be closer to the physical phenomena exception in *Funk Bros.*, which invalidated a patent that essentially claimed the mutual lack of inhibition between two species

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121 *Cf., e.g.*, *supra* note 108 (discussing Moore v. Regents of the Univ. of Cal., 793 P.2d 479, 489 (Cal. 1990)).

122 Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) ("[R]espondent's micro-organism plainly qualifies as patentable subject matter. His claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occuring manufacture . . . .").

123 *See id.* at 309 (providing generic examples of exceptions to patentability).

124 *See* Bilski v. Kappos, 130 S. Ct. 3218, 3231 (2010) (holding that hedging is an abstract idea outside the realm of patentability).

of bacteria.[125] One can argue that the embryonic stem cell researchers did not create the state of pluripotency. Instead, pluripotency is an inherent quality of these cells. Thus, it is merely, in the words of the Court, "the work of nature."[126] This reasoning would place embryonic stem cells outside of the realm of patentability. However, this rationale seems overly simplistic given the drastic implications of such a decision because it would invalidate all patents over pluripotent cells and because it is difficult to place the inventions in any particular category that bars patentability. Instead, it may be more useful to analyze patentability through the "inventiveness" filter.[127]

When adjudicating inventiveness, the first question is whether embryonic stem cells involve sufficient use of the "inventive faculty" to allow for patentability.[128] As explained, embryonic stem cells are taken from the inner cell mass of the pre-implantation blastocyst, an early stage of fetal development.[129] Thus, they do exist in some form in nature. In fact, when tested, the inner cell mass displays the same identification markers as *in vitro* embryonic stem cells.[130] Therefore, in order for patents on stem cells to be inventive, some use of creativity must be employed in the invention itself. Patent applicants can argue that isolating the cells from their natural state and getting them to grow in a laboratory, *ex utero*, requires some creativity: There are many factors and uncertainties that can affect the survival of these cells, so success demonstrates ingenuity in the isolated embryonic stem cell invention. While there is some truth to this, the embryonic stem cell invention may be compared to a biologist going into the rainforest and discovering a previously unknown insect: The insect may be difficult and expensive to grow outside of its natural habitat, but when the biologist finally does learn the optimal conditions for growing the insect, she would not be able to claim the insect itself in a patent. The biologist may claim the *method of growing* the insect in the laboratory, because this is the creative invention that resolves the

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125 *See* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130–31 (1948) (describing the invention in the case).

126 *Id.* at 130.

127 *See supra* Part I.B.2 (introducing inventiveness).

128 *See supra* notes 78–80 and accompanying text (discussing "inventive faculty").

129 *See supra* note 97 (discussing the source of embryonic stem cells).

130 *See, e.g.*, C. Hansis et al., *Oct-4 Expression in Inner Cell Mass and Trophectoderm of Human Blastocysts*, 6 MOLECULAR HUM. REPROD. 999, 999 (2000) ("Oct-4 is highly expressed in human ICM cells."); M.B. Morris et al., *Biology of Embryonic Stem Cells*, *in* HUMAN EMBRYONIC STEM CELLS 1, 4–5 (J. Odorico et al. eds., 2005) (describing Oct-4 expression in embryonic stem cells and noting that "*Oct4* in the embryo is expressed in the inner cell mass cells of the blastocyst").

difficulties encountered in growing the insect outside of the rainforest, but such claims would not cover the insect itself.[131]

The inventiveness inquiry shifts somewhat upon considering that existing stem cell patents claim an *in vitro* "preparation" of cells with some additional limitations such as the ability of the cells to proliferate in culture for over a year and maintain their pluripotency.[132] These purified preparations are not found in nature in exactly the same form as they are claimed, which leads to asking whether, in the words of *Chakrabarty*, these cells are "markedly different" from their naturally occurring counterparts.[133] The answer is not completely clear. Militating against patentability, both the naturally existing and patented stem cells display pluripotency, which is the most important aspect of the invention because without this quality the stem cells would have very limited therapeutic potential. On the other hand, a difference supporting patentability is the fact that the cells in the embryo do not maintain their pluripotent state: The fetus develops into a newborn human being with a full complement of differentiated cell types.

Yet this argument for patentability loses force when one considers that the embryonic stem cells in the inner cell mass would maintain their pluripotent state for an extended period of time if the environment in the uterus permitted it. A culture of embryonic stem cells offers stable growing conditions for the cells in which they may maintain their pluripotent state *in vitro*, a situation equivalent to a hypothetical static uterine environment. Furthermore, *in vitro* embryonic stem cells display the same gene transcription regulators and express the same stage-specific proteins as cells in the inner cell mass.[134] Balancing these arguments against the mere difference in

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[131] Clearly this argument is applicable to methods of growing stem cells in the laboratory. *See infra* note 148 and accompanying text (discussing patents for methods of culturing stem cells).

[132] For example, claim 1 of the '806 Patent is for:

> [a] purified preparation of pluripotent human embryonic stem cells which (i) will proliferate in an *in vitro* culture for over one year, (ii) maintains a karyotype in which the chromosomes are euploid and not altered through prolonged culture, (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) is inhibited from differentiation when cultured on a fibroblast feeder layer.

U.S. Patent No. 6,200,806 col.21 ll.1–9 (filed June 26, 1998). Similarly, the 7,955,851 Patent claims an embryonic stem cell culture grown "on an extracellular matrix in a culture medium" and names two compounds that are to be found in the medium. U.S. Patent No. 7,955,851 col.34 ll.6–8 (filed Sept. 21, 2009).

[133] Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).

[134] *See* Tamar Dvash et al., *Human Embryonic Stem Cells as a Powerful Tool for Studying Human Embryogenesis*, 60 PEDIATRIC RES. 111, 114–15 (2006) (describing similarity in gene expression between early human embryogenesis and embryonic stem cells);

location between cultured and *in utero* cells supports the conclusion that cultured embryonic stem cells are not markedly different from the naturally occurring pluripotent cells and as a result are not patent eligible.[135]

Additionally, the reasoning of a majority of the judges from the Federal Circuit panel in *Myriad*, which discussed the patentability of isolated DNA,[136] supports the conclusion that embryonic stem cells are not patentable subject matter. Judge Lourie's opinion for the court focused on the chemical nature of Myriad's claimed DNA in assessing whether it has markedly different characteristics than the DNA found in cells and specifically used "covalent bonds" as the indicia of "'markedly different' characteristics."[137] This approach would likely support the conclusion that *in vitro* embryonic stem cells are not different enough from *in utero* embryonic stem cells to be patentable subject matter: Neither set of cells has chemical bonds connecting them to other cells,[138] and, as previously explained, embryonic stem cells have the same identity as inner cell mass cells in terms of the markers they display and their transcription factors, thus lacking the

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Morris et al., *supra* note 130, at 3–5 (discussing similarities between embryonic stem cells and cells of the inner cell mass). For more on transcription regulators, see generally Juan M. Vaquerizas et al., *A Census of Human Transcription Factors: Function, Expression and Evolution*, 10 NATURE REVS. GENETICS 252 (2009). For additional information on the significance of stage-specific proteins, see generally James A. Thomson & Jon S. Odorico, *Human Embryonic Stem Cell and Embryonic Germ Cell Lines*, 18 TRENDS IN BIOTECH. 53 (2000). Some differences between *in utero* and *in vitro* embryonic stem cells that do not constitute "marked differences" include the fact that cells of the inner cell mass are surrounded by the trophoblast and grow in suspension, whereas *in vitro* embryonic stem cells adhere to the tissue culture dish (though not completely in a monolayer) and are not surrounded by other cell types.

135 Professors Demaine and Fellmeth's inventiveness test would reach the same result in this case because the biological function of *in vitro* embryonic stem cells is the same as it is when the cells are in the inner cell mass. *See* Demaine & Fellmeth, *supra* note 19, at 406 (summarizing the authors' test). *But see* Korobkin & Munzer, *supra* note 120, at 49–55 (arguing that these differences are significant enough for patentability).

136 Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 653 F.3d 1329 (Fed. Cir. 2011), *petition for cert. filed sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 11-725 (U.S. Dec. 7, 2011). For a discussion of the case, see *supra* notes 69–75 and accompanying text.

137 *Myriad*, 653 F.3d at 1352–53.

138 That is, inner cell mass cells in the *in utero* blastocyst are not bonded to cells outside of the inner cell mass, and *in vitro* embryonic stem cells have no bonds either. It should be noted, however, that gap junctions (channels connecting cells) do exist in the pre-implantation embryo. *See generally* Franchesca D. Houghton, *Role of Gap Junctions During Early Embryo Development*, 129 REPROD. 129 (2005) (providing an overview of the role of gap junctions in the developing embryo). Unlike chemical bonds, removing gap junctions does not change the identity of the cells forming the junctions. Thus they are distinct from chemical DNA bonds in *Myriad* and are not pertinent to this inquiry.

critical difference identified by the *Myriad* majority.[139] Similarly, the reasoning of Judge Bryson's *Myriad* dissent, which analyzed patentability in terms of a manufacture's change in character or function from its preexisting state,[140] would also support the conclusion that embryonic stem cells are not patentable. A similarly thinking judge might view an embryonic stem cell patent as involving the "purification" of cells from an embryo and would focus on the innate *in vitro* potential of the cells rather than their *in utero* potential.[141] Since in both situations the cells are pluripotent, the cells are likely to be found unpatentable under Judge Bryson's reasoning.

On the other hand, Judge Moore's logic, which focused on the difference in "the ends nature originally provided,"[142] may uphold claims on embryonic stem cells. This view considers actual utility to researchers and industry. As Judge Moore explained, "[c]reating isolated DNA allows a scientist, among other things, to remove potentially confounding sequences that are naturally present in the larger chromosomal polymer, and instead focus on just the sequence of interest."[143] Likewise, embryonic stem cells grown in culture can be used as the basis for therapies—a utility that inner cell mass cells do not have—which would render these cells patent eligible under Moore's test.[144]

Some argue that this reasoning is flawed because it conflates the utility requirement with the patentable subject matter requirement.[145] If utility were the only concern for patentability, some seminal patentable subject matter cases would have come out the other way: Claims for using abstract ideas in *Flook* and *Bilski* and natural phenomena in *Funk Bros.* would be deemed patent eligible for providing a novel way to achieve a useful result. Judge Moore's view also assumes that purified products of nature are patent eligible simply because they are purified and made more useful or accessible. But, as previously explained, the Court's precedent does not support this view.[146]

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[139] *See supra* note 130 and accompanying text (describing markers); note 134 and accompanying text (describing the importance of transcription factors).

[140] *See Myriad*, 653 F.3d at 1377–78 (Bryson, J., dissenting) (explaining an alternative patentability analysis).

[141] *Cf. id.* at 1376–78 (discussing DNA claims).

[142] *Id.* at 1359 (Moore, J., concurring) (quoting Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131–32 (1948)) (internal quotation marks omitted).

[143] *Id.* at 1363.

[144] *Cf. id.* at 1365 (discussing the diagnostic testing utility of isolated DNA as compared to natural DNA).

[145] *See, e.g.*, Demaine & Fellmeth, *supra* note 19, at 338–39 (criticizing tests that conflate utility with newness).

[146] *See supra* notes 55–56 and accompanying text (describing precedent on purification inventions).

Therefore, from a purely legal point of view, embryonic stem cells do not comprise patentable subject matter. When they are eventually tested in litigation, these patents should not survive the scrutiny of the courts.

Nonetheless, there are certain types of cells that may be patent eligible. For example, a few years ago scientists discovered ways to produce induced pluripotency stem (iPS) cells, which function like "synthetic" embryonic stem cells but are not taken from developing embryos. To make iPS cells, scientists take cells from living adults and perform a laboratory process to make them resemble embryonic stem cells.[147] Since iPS cells are not found naturally in any form, they are analogous to the new bacteria in *Chakrabarty* and should be patentable. Additionally, corporations could (and do) patent methods and media for culturing embryonic stem cells.[148] Neither of these inventions is preemptive because scientists are able to create new types of iPS cells and methods of culturing embryonic stem cells—that is, they can invent around these patents. Thus, there remains room for patents in the field without claiming embryonic stem cells themselves.

B. The Patent Ineligibility of Stem Cell Differentiation Methods

The second group of patents addressed in this Note comprises methods of controlling the differentiation of embryonic stem cells into other cell types of the body. These include methods for differentiation into hematopoietic cells, neural cells, endoderm, and cardiomyocytes, among others.[149] These method patents disclose and claim general procedures involving growth of embryonic stem cells in a medium containing specific chemical compounds, usually proteins. For

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[147] *See generally* Kazutoshi Takahashi et al., *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 CELL 861 (2007) (reporting the derivation of iPS cells from human subjects); Kazutoshi Takahashi & Shinya Yamanaka, *Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors*, 126 CELL 663 (2006) (describing the derivation of iPS cells from mice).

[148] This is analogous to the methods of growing the insect in *supra* note 131 and accompanying text. Preemption concerns are insignificant for these patents because there are many potential ways to maintain an embryonic stem cell culture and these methods and media are distinct from anything found in nature, unlike differentiation methods, which actually employ natural processes, as explained *infra* Part III.B.

[149] A sampling of the patents includes the following: U.S. Patent No. 7,772,001 (filed Jan. 3, 2006) (endoderm differentiation); U.S. Patent No. 7,452,718 (filed Mar. 21, 2005) (cardiomyocyte differentiation); U.S. Patent No. 7,332,336 (filed Feb. 27, 2004) (hepatocyte differentiation); U.S. Patent No. 7,413,903 (filed Sept. 9, 2003) (method for inhibiting differentiation); U.S. Patent No. 6,613,568 (filed Aug. 27, 2001) (hematopoietic differentiation); U.S. Patent No. 6,833,269 (filed May 31, 2001) (neural differentiation). Similar patents have been filed but not yet granted. *See, e.g.*, U.S. Patent Application No. 12/134,521 (filed June 6, 2008) (neural differentiation). Patent applications are published eighteen months after they are filed if they are not yet granted. 35 U.S.C. § 122(b) (2006).

example, U.S. Patent No. 6,833,269 calls for "culturing [human embryonic stem] cells in a medium containing one or more added neutrophins and one or more added nitrogens" to produce a population of neural cells,[150] and U.S. Patent No. 7,452,718 claims a method for growing the embryonic stem cells "in the presence of activin and a bone morphogenic protein to produce cardiomyocyte lineage cells."[151] Sometimes these methods also include a step in which the cells must be plated on a tissue culture dish, but experience has shown that such steps do not truly affect the ability of the cells to differentiate.[152]

Determining whether differentiation methods are patentable subject matter requires a basic primer on developmental biology, the science underlying these inventions. The fact that developing embryos are in the uterus and cannot be observed directly limits our understanding of embryonic development. Scientists cannot conduct biomolecular tests to observe cellular receptors on the cells in the embryo as this would require aborting the developing embryo purely for research purposes.[153] Thus, much of what is known about embryonic development comes from mouse models, which allow scientists to directly observe the embryo at any stage of development.[154] Studies

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[150] '269 Patent col.32 ll.56–58.

[151] '718 Patent col.28 ll.9–11. Similarly, the '568 Patent claims a method of "exposing a human embryonic stem cell culture to mammalian hematopoietic stromal cells so as to thereby produce human hematopoietic cells." '568 Patent col.8 ll.54–56. Stromal cells, which are connective tissue cells, release proteins into the medium, which is essentially the same as having a scientist add the compounds. *See, e.g.*, Hiroshi Kawasaki et al., *Induction of Midbrain Dopaminergic Neurons from ES Cells by Stromal Cell–Derived Inducing Activity*, 28 NEURON 31, 36–37 (2000) (discussing the use of stromal cells in the context of neuronal differentiation). The difference between using stromal cells to release compounds and scientists directly releasing compounds is that researchers may not know all the compounds released by stromal cells and as a result may be unable to replicate exposure to stromal cells with pure, defined factors in the laboratory.

[152] *Compare* Su-Chun Zhang et al., *In Vitro Differentiation of Transplantable Neural Precursors from Human Embryonic Stem Cells*, 19 NATURE BIOTECH. 1129 (2001) (differentiating using a suspended culture), *with* Lesley Gerrard et al., *Differentiation of Human Embryonic Stem Cells to Neural Lineages in Adherent Culture by Blocking Bone Morphogenetic Protein Signaling*, 23 STEM CELLS 1234 (2005) (differentiating in an adherent culture).

[153] Note, however, that after obtaining informed consent, scientists routinely conduct tests on aborted fetuses and use cells from these fetuses for research purposes. *E.g.*, Steven H. Lewis et al., *HIV-1 in Trophoblastic and Villous Hofbaur Cells, and Haematological Precursors in Eight-Week Fetuses*, 335 LANCET 565 (1990) (using aborted fetuses to study the vertical transmission of HIV-1). This source of cells is inadequate for scientific experimentation because there is a limited number of such fetuses, some aborted fetuses have genetic abnormalities (due to which they were aborted), and the cells do not survive indefinitely in culture.

[154] *See* Tamar Dvash & Nissim Benvenisty, *Human Embryonic Stem Cells as a Model for Early Human Development*, 18 BEST PRACTICE & RES. CLINICAL OBSTETRICS & GYNECOLOGY 929, 930–31 (2004) (explaining the physiological and molecular similarities

on mice have shown that *in utero* differentiation is fostered by signaling between cells, which, in turn, requires undifferentiated cells to have receptors for the signals that reach them.[155] The genes that code for these receptors, and all other cellular functions, are similarly expressed both in mouse and human embryonic stem cells.[156] Therefore, cellular signals are thought to have the same effects on embryonic stem cells *in vitro* as they do on their *in utero* equivalents. This is why scientists use human embryonic stem cells as an *in vitro* model for human fetal development.[157]

In fact, this similarity between early mammalian development and embryonic stem cells has guided scientists in their quest to direct the differentiation of embryonic stem cells: Scientists have sought to apply their knowledge about embryonic development *in utero* by manipulating the same signaling pathways in embryonic stem cells *in vitro*.[158] For example, in inducing neural differentiation for the first time, scientists added two compounds to the growth medium, "bFGF" and "EGF," which were known to affect neural cell proliferation in other embryonic cells.[159] Likewise, for directing differentiation to pancreatic cells, scientists used retinoic acid "[b]ased on the findings that [retinoic acid] signaling is necessary for pancreatic specification during" early embryonic development.[160]

Not surprisingly, patents claiming methods of differentiation use the same compounds as those discovered by scientists based on their knowledge of *in utero* embryonic development: For neural differentia-

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between human and mouse development and reasons why mice are a good surrogate model for human development).

[155] *See* Charles E. Murry & Gordon Keller, *Differentiation of Embryonic Stem Cells to Clinically Relevant Populations: Lessons from Embryonic Development*, 132 CELL 661, 662, 667 (2008) (describing the "signaling environments that are responsible for the induction of specific" cell types).

[156] Dvash et al., *supra* note 134, at 114 (describing cDNA microarray studies).

[157] For two excellent review articles summarizing and explaining the importance of this use of embryonic stem cells, see generally Dvash & Benvenisty, *supra* note 154; Dvash et al., *supra* note 134. *See also* Ludovic Vallier et al., *Early Cell Fate Decisions of Human Embryonic Stem Cells and Mouse Epiblast Stem Cells Are Controlled by the Same Signalling Pathways*, 4 PLOS ONE e6082, e6082 (2009) (analyzing the effect of widely studied developmental growth factors on cell differentiation decisions in human embryonic stem cells).

[158] *See* Czyz & Wobus, *supra* note 106, at 167 ("The recapitulation of developmentally regulated gene expression patterns enables the analysis of developmental processes on a cellular level in vitro."); Murry & Keller, *supra* note 155, at 661–63 (describing researchers' application of knowledge from embryonic development to embryonic stem cells).

[159] Benjamin E. Reubinoff et al., *Neural Progenitors from Human Embryonic Stem Cells*, 19 NATURE BIOTECH. 1134, 1135 (2001).

[160] Shim et al., *supra* note 105, at 1231.

tion, "bFGF" and "EGF" can be used,[161] and for pancreatic differentiation, retinoic acid is an important factor in the medium.[162] Therefore, differentiation patents are quite plainly the same processes that occur naturally in the developing embryo, except translated to the laboratory environment. This means that the differentiation methods, like the natural reaction between the bacteria in *Funk Bros.*, are natural phenomena and consequently fall under one of the categorical exclusions to patentability.[163]

Additionally, both the inventiveness and preemption tests weigh against the patentability of these methods of differentiation. With regard to inventiveness, the underlying natural principle is the way in which cells in the developing embryo differentiate, so any claimed method must add some use of the "inventive faculty" to this already existing phenomenon. As explained above, patents on differentiation methods (or at least pure differentiation claims) are mere applications of signaling pathways from embryonic development, so in order to be inventive they must do more than simply use the discoveries of these natural processes. The only part of these inventions that may add anything to the natural phenomena is the part claiming the differentiation for *embryonic stem cells* as opposed to cells *in the embryo*.[164] Yet, this fact should not make these differentiation methods patentable because it merely "limit[s] the use of the [naturally occurring method] to a particular technological environment"[165]—the *in vitro* embryonic stem cell system. As a result, there is no inventive addition to the natural phenomenon.[166]

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161 *E.g.*, U.S. Patent No. 6,833,269 col.32 ll.66–67 to col.33 ll.1–3 (filed May 31, 2001) (claiming the use of a combination of bFGF and EGF).

162 *E.g.*, U.S. Patent Application No. 12/183,557, at 1, 7, 12 (filed July 31, 2008).

163 An important distinction must be made for patents claiming differentiation by use of laboratory-made small molecules that are not involved in the natural differentiation process. *See, e.g.*, U.S. Patent Application No. 12/747,116 (filed Dec. 11, 2008) (claiming a pyridine analog used for neuronal differentiation). Since these patents do not claim the same compounds as those that are naturally employed in cellular differentiation, they are not natural phenomena and should be patentable.

164 Not all of these patents or applications restrict their claims to embryonic stem cells. *Compare* U.S. Patent No. 7,772,001 col.39 ll.2–3 (filed Jan. 3, 2006) (claiming "differentiation of human embryonic stem cells"), *with* U.S. Patent Application No. 12/183,557, at 13 (filed July 31, 2008) (claiming differentiation of "pluripotent" stem cells, which may be read to encompass cells in the actual embryo).

165 Bilski v. Kappos, 130 S. Ct. 3218, 3230 (2010) (quoting Diamond v. Diehr, 450 U.S. 175, 191 (1981)) (internal quotation marks omitted). Similarly, one may frame the problem as the differentiation of the pluripotent cells, such that the use of this particular cellular environment is merely a post-solution step. *See* Parker v. Flook, 437 U.S. 584, 590 (1978) (explaining the unpatentability of post-solution steps).

166 The importance of the differentiation patents is the process of differentiating, not the *in vitro* environment. Justice Breyer addressed a similar issue in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124, 125 (2006) (Breyer, J.,

Similarly, differentiation methods are not patentable because they are not markedly different from natural differentiation processes. In fact, they are exactly the same. Unlike in *Chakrabarty*, where the new bacteria did not exist in nature in any form, the claimed differentiation processes occur *in utero* in the inner cell mass.[167] And, while the cellular environment certainly differs between embryonic stem cells and the blastocyst,[168] these claims fail even under the broad definition of "markedly different" adopted in *Myriad*.[169] Recall that in *Myriad*, the marked difference in Judge Lourie's opinion for the court was based upon the chemical nature of isolated DNA as compared with natural DNA.[170] This may have been reasonable, given that the claimed invention was isolated DNA, which by itself has different chemical properties from cellular DNA. In the case of differentiation, however, the invention is the differentiation process as it occurs *in* the embryonic stem cells. This means that the chemical identity of the cellular environment need not matter for the markedly different analysis. In simpler terms, even if there were a chemical difference (i.e., the metric used by the *Myriad* Court) between embryonic stem cells and cells in the blastocyst, this difference should not allow patentability for differentiation methods. This is because there is no chemical difference between the differentiation *process* itself in the blastocyst and in the laboratory-grown embryonic stem cell.

The result is the same when patentable subject matter eligibility is viewed through the lens of preemption. Here, the concern is whether the differentiation method claims cannot be invented around and thus prevent others from utilizing the natural principles involved.[171] Proponents of patentability can argue, using language from *Diamond v.*

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dissenting from dismissal of certiorari). The patent in that case was for a method of detecting a patient's vitamin deficiency by examining the level of an amino acid in the patient's blood. *Id.* In response to the patentee's argument that the method was patentable because it involved a transformation of the patient's extracted blood, Justice Breyer pointed out that the patent itself "is *not* a process for transforming blood," so it is irrelevant that such steps are added to the patent—it remains unpatentable even with them. *Id.* at 136.

[167] By themselves, the differentiation processes do not have "markedly different characteristics from any found in nature." Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980).

[168] The blastocyst forms several days after fertilization and after various cell divisions and "is comprised of an outer layer of cells and an inner cell mass." Miller, *supra* note 119, at 558–59.

[169] Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 653 F.3d 1329, 1351 (Fed. Cir. 2011), *petition for cert. filed sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., No. 11-725 (U.S. Dec. 7, 2011).

[170] *See supra* notes 136–39 and accompanying text (describing Judge Lourie's opinion for the court).

[171] *See* Dreyfuss & Evans, *supra* note 44, at 1352 (explaining preemption); *supra* Part I.B.1 (discussing preemption).

Diehr, that these patents do not preempt the use of the actual differentiation process because there are specific applications and specific laboratory conditions that are contemplated by these patents, thus preserving the ability of others to "work around" these methods by going outside the particular claimed application.[172] Yet, a stronger argument against patentability may be found in *Bilski*, where the Court held that the claims over hedging were unpatentable because they would preempt the "use of [hedging] in all fields, and would effectively grant a monopoly over an abstract idea."[173] Once the preemptive effect of the broad claims was established, the Court held that even the more limited claims, which restricted hedging to the energy market, were not patentable subject matter because they did not add anything to the basic hedging claims.[174] By analogy, a claim over a method for differentiating any pluripotent cell would be a patent over a natural phenomenon that would preempt the use of this phenomenon in any application. Thus, limiting the method to *in vitro* embryonic stem cells would not necessarily allow such claims to overcome the patentability hurdle.[175]

Understanding the Court's thinking in this way is important for the analysis in this Note because embryonic stem cells may not be the only medium in which these differentiation techniques may be employed. For example, recall iPS cells, the "synthetic" embryonic stem cells previously described.[176] Even though iPS cells can be differentiated in the same ways as embryonic stem cells, the existing patents over differentiation processes would not preempt the use of the methods in iPS cells. This is because the patents claim differentiation of embryonic stem cells rather than any pluripotent cells. Yet, applying natural differentiation methods to iPS cells is not inventive for the same reasons that it is not inventive to apply them to embryonic stem cell differentiation. Therefore, preemption by itself, at least when understood to mean preemption of the natural process for any particular application, is not sufficient for denying patentability over

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172 *See* Diamond v. Diehr, 450 U.S. 175, 187 (1981) (giving reasons why the invention in that case was patentable subject matter). As explained by the Court in the *Telephone Cases*, limiting a patent's claims over a natural phenomenon to a specific application can allow patentability. 126 U.S. 1, 533–34 (1888); *see supra* note 51 (discussing the *Telephone Cases*).

173 Bilski v. Kappos, 130 S. Ct. 3218, 3231 (2010).

174 *Id.*

175 The *Bilski* Court's reasoning essentially combines the preemption and inventiveness analyses into two steps: Preemption is used to deal with broader claims, and once it is established, an inventiveness analysis can exclude more specific applications of the broad claims, which by themselves are not preemptive.

176 *See supra* notes 147–48 and accompanying text.

these processes, as long as the patents in question do not claim differentiation methods for all pluripotent cells. Instead, differentiation methods specific to embryonic stem cells must be analyzed under both the preemption and inventiveness tests in order to be found ineligible for patentability.[177]

Overall, the law of patentable subject matter militates against allowing patents for either embryonic stem cells or methods of differentiating these cells. In addition, there are extralegal policy reasons supporting this result. These policy reasons are discussed in the following Subpart.

C. Policy Reasons for Denying Stem Cell and Differentiation Patents

In addition to the legal reasons for which patents over embryonic stem cells and differentiation processes should be denied, there are also strong policy justifications for holding the same view. This Subpart focuses on two related justifications: first, the needs of academics and medical researchers who want to use stem cells in their laboratories, and second, incentivizing innovation.[178] Both of these justifications advise against allowing stem cell patents.

1. Potential Infringement Liability Deters Researchers

The basic policy question to be addressed is whether patents over embryonic stem cell technologies foster or impede innovation in the field. Given that innovation is complex and builds on prior work,[179] exclusivity from patents may slow down follow-on innovation,[180] which is required for stem cell therapies to reach the market. For example, as explained in Part II, stem cell and differentiation process

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[177] Since iPS cells may eventually prove to have as much potential as embryonic stem cells, this is a more difficult case in which to apply Professors Dreyfuss and Evans's view of preemption as reflecting the inability of others to invent around the patented invention. *See* Dreyfuss & Evans, *supra* note 44, at 1361. Simply because there may be other ways to achieve differentiation of pluripotent cells (by not using embryonic stem cells) does not mean that these patents should be granted. Instead, one must phrase the inquiry in terms of both preemption and inventiveness. Professors Dreyfuss and Evans recognize that the inventing-around standard is sometimes difficult to apply because it requires an intimate grasp of the field in question and a contextual understanding of the invention. *Id.* at 1372.

[178] This Note does not discuss moral concerns regarding these patents as this issue has been analyzed in depth in the literature. For a list of sources, see *supra* note 118.

[179] *See* Katherine J. Strandburg et al., *Law and the Science of Networks: An Overview and an Application to the "Patent Explosion,"* 21 BERKELEY TECH. L.J. 1293, 1340, 1342 (2006) (explaining the complexity of innovation and ways in which old technologies are important for inventing new technologies).

[180] *See generally* Kenneth G. Huang & Fiona E. Murray, *Does Patent Strategy Shape the Long-Run Supply of Public Knowledge? Evidence from Human Genetics*, 52 ACAD. MGMT. J. 1193 (2009) (describing the impact of patents on follow-on innovation).

patents cover basic concepts and tools that scientists use in researching therapies that involve embryonic stem cells. This means that patentees who own the rights to these cells or processes may use their right to exclude, by threat of lawsuits, in order to prohibit all scientists and academic researchers from using the patented inventions in their work. Such threats may stymie efforts to develop stem cell therapies.

This unfortunate result derives from the fact that the American patent system does not exempt noncommercial and purely academic research from liability.[181] The Federal Circuit gives a very narrow construction to the common law experimental-use exemption: In *Madey v. Duke University*, the Federal Circuit essentially made it impossible for university and clinical researchers to use the exemption as a shield from infringement liability.[182] The *Madey* court reasoned that such research "unmistakably further[s] the institution's legitimate business objectives, including educating and enlightening students and faculty participating in" research projects.[183] Because university research is considered a business activity, it cannot be noncommercial or purely philosophical as required for the exemption.[184] Additionally, these research scientists likely cannot seek protection under the separate statutory exemption from infringement liability that only protects research "reasonably related" to FDA regulation.[185]

The consequence is that university scientists who want to develop ways to reach the full potential of embryonic stem cells face the prospect of being held liable for infringing patents regardless of whether these scientists seek to commercialize their discoveries. This is true even if the sole purpose of university scientists' research is to invent around patented methods,[186] which may be the case if they want to

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[181] Given the vast literature explaining the exemptions from liability, I do not provide an overview of this subject. For a history of the experimental-use exemption, see Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 93–100.

[182] *See* 307 F.3d 1351, 1362 (Fed. Cir. 2002) (noting that the experimental-use defense is "narrow and strictly limited").

[183] *Id*.

[184] *Id.* at 1361–62. Most academic literature has criticized this narrow view. *Cf.* Alan Devlin, *Restricting Experimental Use*, 32 HARV. J.L. & PUB. POL'Y 599, 605 n.27 (2009) (citing articles that criticize the court's narrow view, but arguing in support of limiting the exemption).

[185] *See* 35 U.S.C. § 271(e)(1) (2006) (laying out the statutory exemption). For background and cases on this exemption, see Katherine J. Strandburg, *The Research Exemption to Patent Infringement: The Delicate Balance Between Current and Future Technical Progress*, *in* 2 INTELLECTUAL PROPERTY AND INFORMATION WEALTH 107 (Peter K. Yu ed., 2007).

[186] *See* Strandburg, *supra* note 181, at 86–87 (discussing a Federal Circuit opinion on the matter).

find new ways to differentiate pluripotent cells and use patented methods as experimental controls. Thus, patents present a real potential for deterring innovation. This is especially true for stem cell and differentiation patents because these patents cover upstream technology that is implicated in any potential therapy and cannot be invented around, while patents over culture methods can be invented around and therefore do not block downstream innovation.[187]

2. Patent Incentives Are Not Necessary for Stem Cell Innovation

Despite the possible deterrent effect on innovation, patents over certain inventions nevertheless could be beneficial if they promote progress more than they impede it. A healthy debate surrounds this question.[188] On one hand, it is clear that patents have some role in incentivizing innovation, which requires monetary investment. Thus "the law must step in to provide a way to recoup such investments or else inventors (or their financial backers) will have insufficient incentive to make research and development investments."[189] On the other hand, some scholars argue that patents are not necessary for innovation, especially when it results from academic research or is not

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[187] Scholars refer to these inventions as "research tool[s]" and have explained that patents over them negatively impact the pace of innovation. *Id.* at 129. Upstream patents may have a greater effect on slowing future innovation in biotechnology than in other industries. *See* David C. Hoffman, Note, *A Modest Proposal: Toward Improved Access to Biotechnology Research Tools by Implementing a Broad Experimental Use Exception*, 89 CORNELL L. REV. 993, 1028–31 (2004) (explaining the importance of upstream patents in biotechnology).

[188] *See generally* DUTFIELD, *supra* note 90, at 325–36 (considering a counterfactual world without patents); Jonathan M. Barnett, *Do Patents Matter? Empirical Evidence on the Incentive Thesis*, *in* HANDBOOK ON LAW, INNOVATION AND GROWTH 178, 178–80 (Robert E. Litan ed., 2011) (discussing both sides of the debate).

[189] Strandburg, *supra* note 181, at 90–91. For further discussion of patent incentives, see *id.* at 90–93. For more on this view, see MATTHEW RIMMER, INTELLECTUAL PROPERTY AND BIOTECHNOLOGY: BIOLOGICAL INVENTIONS 3 (2008). Professors Abramowicz and Duffy link patents' effect on innovation to the length of exclusivity. Michael Abramowicz & John F. Duffy, *The Inducement Standard of Patentability*, 120 YALE L.J. 1590, 1626–27, 1647–48 (2011). Abramowicz and Duffy also note that patents do seem to help with commercialization. *Id.* at 1647–48. Applying the incentive idea to other areas of law, Professors Putnam and Tepperman argue that all intellectual property rights promote progress and "stimulat[e] productive economic activity." Jonathan D. Putnam & Andrew B. Tepperman, *Intellectual Property Rights and Economic Progress*, *in* HANDBOOK ON LAW, INNOVATION AND GROWTH, *supra* note 188, at 112, 113.

directly commercializable.[190] Other scholars go as far as writing that patents may actually impede progress.[191]

The view that patents are not required for innovation may have especially strong footing in the stem cell field. First, most life science researchers are academics who may be more concerned with their academic publications than with patents issued in their name. As a result, these researchers may do what they can to publish, even if it means foregoing a patent.[192] The Department of Health and Human Services specifically looked at this issue in the context of patents over genes and genetic tests. It concluded that scientists would have conducted research in these fields regardless of the patent eligibility of their discoveries.[193] Second, government grants make up a large percentage of

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[190] *See, e.g.*, Barnett, *supra* note 188, at 180 ("[P]atents are usually not a strictly 'but for' condition behind a firm's decision to invest in an innovation project . . . ."); Margaret Chon, *Intellectual Property and the Development Divide*, 27 CARDOZO L. REV. 2821, 2881 (2006) ("[T]here are many ways to incentivize innovation [other] than to automatically privatize goods through a scheme of exclusive rights such as patent or copyright."); Petra Moser, *How Do Patent Laws Influence Innovation? Evidence from Nineteenth-Century World's Fairs*, 95 AM. ECON. REV. 1214, 1214–17 (2005) (laying out arguments in the incentive debate). Professor Dutfield hypothesizes that "scientific and technological advances . . . would have developed pretty much as they did with or without patents." DUTFIELD, *supra* note 90, at 328; *accord* SHIVA, *supra* note 89, at 13–15 (discussing the motivations of academic researchers).

[191] One classic paper holding this view discusses the threat of anticommons in biomedical research. *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998). According to Professor Barnett, the problem stems from the transaction costs associated with individual property rights. Barnett, *supra* note 188, at 203; *see also* Bilski v. Kappos, 130 S. Ct. 3218, 3255 (2010) (Stevens, J., concurring) (noting that certain patents "may prohibit a wide swath of legitimate competition and innovation"). On a related note, Professors Demaine and Fellmeth point out that "[t]here is a serious concern . . . that the patent monopolies resulting from commercialization of preexisting natural products skew academic research toward lucrative biotechnological cures rather than more conventional therapies or research into the underlying causes of disease." Demaine & Fellmeth, *supra* note 19, at 433 n.570.

[192] *See* College of Medical Genetics Brief, *supra* note 53, at 14 ("Patents are not needed to incentivize this study of clinical correlations and would stifle rather than incentivize developments in the practice of personalized medicine."); Holbrook, *supra* note 90, at 31 ("Academic papers contain [intellectual property rights], in that the authors are claiming priority of discovery.").

[193] DEPT. HEALTH & HUMAN SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 20–21 (2010) ("Scientists interviewed as part of the case studies stated that they would have pursued their research even if their discoveries were not patent-eligible. . . . Rather, they stated that the [research] races were driven by wanting priority of scientific discovery, prestige, [and] scientific credit . . . ."). For a list of factors motivating researchers, see Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1585 (2003). These motivations make such researchers less like "seller" innovators and more like "user" innovators, who may not need patents to motivate their innovation. *See* Katherine J. Strandburg, *What If There Were a Business Method Use Exemption to Patent Infringement?*, 2008 MICH. ST. L.

biotechnology research funding,[194] which means that even if private entities do not invest in the research, it will nonetheless continue.[195]

At the same time, however, due to the financial riskiness of biotechnology, patent protection may be essential if the goal is not only to invent but also to bring to market new therapies, including stem cell–based cell replacement therapies.[196] Biotechnology firms may need assurances that they will have no direct competitors in order to be incentivized to invest in stem cell–based therapies. Moreover, although biotechnology firms may receive this security from patents over the therapies, the protection will be significantly broader, and perhaps more conducive to investment, if it can include the differentiation methods or stem cells as well.

I believe that patents over stem cells and differentiation processes are not required in order to promote research into therapies that utilize stem cells. Academic researchers will continue their work in building the basic steps upon which therapies will be based, such as techniques to more efficiently differentiate embryonic stem cells in ways that ensure their post-surgery survival and proliferation in the patient. Patents do not incentivize these researchers. If private corporations wish to be the only players in the market for certain stem cell–based therapies, there are other patentable options. For example, corporations may patent particular surgical or other treatment techniques used on patients. This would allow these corporations to reap rewards from the development of actual therapies. Given the deterrent effects of the almost nonexistent research exemption, patents over stem cells and differentiation processes may impede progress in

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REV. 245, 265–67 (explaining the distinction between the two terms in light of innovation incentives).

194 E. Ray Dorsey et al., *Funding of US Biomedical Research, 2003–2008*, 303 J. AM. MED. ASSOC. 137, 140 (2010) ("Federal sources remain the largest contributor to academic biomedical research expenditures, accounting for 65% of expenditures, followed by institutional funds (18% of expenditures)."); Holman, *supra* note 68, at 2 ("To a large extent . . . fundamental discoveries come out of university and publicly funded research . . . ."); Mireles, *supra* note 119, at 1178–81 (discussing state-initiated funding for stem cell research); Miller, *supra* note 119, at 575 ("[G]overnment funding of [stem cell] research is skyrocketing."). For a study investigating the impact of funding on innovation, see Jeffrey L. Furman et al., *Growing Stem Cells: The Impact of US Policy on the Geography and Organization of Scientific Discovery* (Mar. 1, 2010) (unpublished manuscript), *available at* http://www2.druid.dk/conferences/viewpaper.php?id=502114&cf=43 (comparing innovation in different countries as correlated with government expenditures on research).

195 This is especially important considering that most stem cell research occurs in universities and hospitals. *See* DUTFIELD, *supra* note 90, at 331 (noting the importance of universities and hospitals to biomedical research).

196 *See* Burk & Lemley, *supra* note 193, at 1588, 1592 (discussing the distinct importance of patent protection for biotechnology and the fact that the biotechnology industry enforces its patents more frequently than other industries).

the field more than they promote it. Therefore, on balance, policy interests weigh against allowing these patents.

Conclusion

This Note concludes that due to the biological processes involved, neither embryonic stem cells nor methods of differentiating these cells qualify for patent protection because they are not patentable subject matter. These patents fail the common law exclusions to patentability as demonstrated by applications of the inventiveness and preemption tests derived from the exclusions. Additionally, policy rationales that account for fostering innovation by academic researchers and allowing widespread access to stem cell–based therapies dictate against granting these patents. Therefore, when litigants finally question the validity of these patents, courts should invalidate them.