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Stem Cell Patents after the America Invents Act

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Under the newly passed Leahy-Smith America Invents Act (AIA), the U.S. Patent and Trademark Office may hear new challenges to stem cell patents. Here, we explore how the new law affects challenges to stem cell patents, focusing on two recent cases, and discuss the future of stem cell patent disputes.

Introduction

Stem-cell-related patents have long been at the center of controversy. Religious groups, patent lawyers, and even other scientists have criticized the process of claiming ownership over the most fundamental of biological building blocks (Golden, 2010). Nonetheless, true legal challenges to the validity or enforceability of many stem cell patents remain rare and are often limited to a narrow subset of current licensees (Plomer et al., 2008). Newly developed administrative procedures at the U.S. Patent and Trademark Office (PTO), however, may change this calculus. Under the Leahy-Smith America Invents Act (AIA), which has been in effect since 2012, the PTO may now hear several types of new challenges to both pending patent applications and already issued patents. These new administrative procedures may be filed by anyone, regardless of the person's legal interest in the patent. This shift may open the door to more frequent—and aggressive—patent challenges by disparate stakeholders against stem cell patents. Interestingly, two recent failed disputes, *BioGatekeeper Inc. v. Kyoto University* and *Consumer Watchdog v. WARF*, illustrate the possibilities—and limits—of this legal development in stem cell patenting. In this Forum, we explore the past state of affairs in stem cell patents, the changes wrought by the AIA (as illustrated by the BioGatekeeper and Consumer Watchdog suits), and the likely future for the security of stem cell patents.

Patent Challenges at the PTO before the AIA

Procedurally, patent disputes typically proceed along one of two paths. The first uses the federal court system to challenge the validity of issued patents. As a matter of constitutional law, all federal court cases must possess an "actual case or controversy:" "that the dispute be 'definite and concrete, touching the legal relations of parties having adverse legal interests'" (MedImmune, Inc. v. Genentech, Inc., 2007). Practically, this means either that the patent holder would first sue an accused infringer directly or that the patent holder would threaten the infringer with a suit such that, for legal purposes, there exists a "substantial controversy" between the parties. The corollary to this maxim, however, is that outsiders who do not live under the threat of being sued have no right to challenge the validity of the patent in federal court. Thus, at least prior to the AIA, challenging the validity of a patent or patent application in federal court was generally limited to those who had a direct, legal interest in the patent: inventors who had been wrongfully left off of the patent application, competitors who had pending patent applications, licensees of the patented technology, or users who had been sued for infringement (Plomer et al., 2008).

The second pathway involves the PTO. Prior to the AIA, several administrative procedures allowed a variety of parties to request that the PTO reconsider patents already issued by the agency. One such procedure, "inter partes reexamination"—available since 1999—allowed any person, at any time, to petition the PTO to reconsider the patent in light of new scientific or technical references that cast doubt on the patent's validity (Tindell, 2007). At the same time, the petitioner was limited to challenging the patent's validity on those references—and not for other technical defects in the patent document. In response, the patent holder could alter its patent's claims at any time to avoid—or delay—further proceedings. Usually, inter partes reexamination functioned as a dispute resolution mechanism for parties with a direct interest in a particular patent: over 75% of all inter partes reexamination requests ever filed concerned patents concurrently being litigated by the same parties in federal court. Furthermore, relative to the pace of federal litigation, disputes tended to drag on, taking 3 years, on average, for the PTO to decide a reexamination proceeding (Love and Ambwani, 2014).

These limits on challenging patents, combined with a robust licensing market, led stem cell patents to be infrequently challenged prior to the AIA (Roberts et al., 2014). The few challenges that did occur mostly concerned University of Wisconsin professor James Thomson's broad, pioneering human embryonic stem cell (hESC) patents (Plomer et al., 2008). There, several prominent scientists objected to the Wisconsin Alumni Research Foundation's (WARF's) aggressive licensing and enforcement strategies. These scientists joined the legal advocacy group The Foundation for Taxpayer and Consumer Rights (now called Consumer Watchdog) to challenge James Thomson's foundational human embryonic stem cell patents before the PTO. Nonetheless, such challenges remained rare. The torpid pace of the inter partes reexaminations further discouraged stem cell inventors from petitioning the PTO to challenge their competitors' patents; advances in the field would likely eclipse the patented technology before the PTO completed its proceedings (Iancu and Haber, 2012). Therefore, stem-cell-related patents remained relatively safe from challenges until the passage of the AIA.

Patent Challenges after the AIA

The AIA may have changed things dramatically. Although it left the requirements for federal litigation largely intact, the Act substantially altered the administrative procedures available to the public to challenge patents at the PTO. First, and foremost, the AIA revamped the old system of inter partes reexamination into a new system of inter partes review. Rather than utilizing an ''amendment and response'' procedure that accounted for much of the old system's delay, the new system proceeds in a quick, trial-type fashion that gives the PTO authority to cancel all of a patent's claims in their entirety. In addition, multiple parties—including members of the public with no legal interest in the patent—may join in the action at the discretion of the PTO. And, while the filing fee for instituting an inter partes review is high—to date, at least $27,500—attorneys' fees for inter partes reviews often cost less than one-tenth of traditional, federal court patent litigation (http://www.mintz.com/newsletter/2014/Advisories/4363-1014-NAT-IP/). The proceedings also take half the time, roughly 15 months from start to finish. Inter partes reviews are also legally easy to initiate and, so far, have been very successful, invalidating over 70% of the patent claims adjudicated at the PTO (Love and Ambwani, 2014).

In addition, anyone may now challenge patents currently before the PTO in what are known as ''preissuance submissions.'' Like the prior system of inter partes reexamination, preissuance submissions allow a third party to submit prior published technical literature useful in assessing—or challenging—the validity of the contested patent, along with a concise description of how the submitted references cast doubt on the patent as written. In contrast to the fee for inter partes reviews, the fees for preissuance submissions are quite cheap: several hundred dollars, depending on the number of references included by the challenger (Iancu and Haber, 2012). Several other administrative challenges have also been created by the AIA—such as covered business method reviews—but it is unlikely that they will greatly affect stem cell patents.

In any event, the AIA's new administrative procedures have been successful insofar as they have allowed greater, faster participation by expanding the criteria for filing trial-type challenges beyond those who are directly threatened by enforcement. So far, more inter partes reviews have been filed since the AIA took effect in 2012 than all of the inter partes reexaminations from 1999–2012. The PTO now also receives, on average, roughly 70 preissuance submissions each month (http://www.law360.com/articles/581512/trends-from-2-years-of-aia-post-grant-proceedings). These numbers appear likely to increase as practitioners become comfortable with the new procedures.

The Consumer Watchdog and BioGatekeeper Challenges

The ease and popularity of administrative patent challenges after the AIA have affected some of the more prominent stem cell technologies. After Consumer Watchdog lost its challenge to WARF's stem cell patents before the PTO, the organization appealed the decision to federal court. There, it asked the U.S. Court of Appeals for the Federal Circuit to apply the U.S. Supreme Court's recent decision on gene patenting, *Association for Molecular Pathology v. Myriad Genetics, Inc.* In *Myriad*, a unanimous Supreme Court held that ''naturally occurring'' DNA segments were not patent eligible, even though they had been ''isolated'' from the surrounding chromosome (Kesselheim et al., 2013). Consumer Watchdog argued that WARF's patents claimed that stem cells were analogous to the isolated DNA segments in *Myriad* because their properties are found in all embryonic stem cells, including their naturally existing counterparts.

But, in its June 2014 decision, the Federal Circuit did not address the substance of Consumer Watchdog's challenge. Rather, it held that because all federal court challenges of patents—even those stemming from the freely open, inter partes review process—required an ''actual case or controversy,'' Consumer Watchdog did not have standing to appeal the PTO's decision. Because WARF never sued or threatened to sue Consumer Watchdog itself, the group had no standing to appeal the PTO's decision; it had suffered no legally apparent injury related to the patent.

Not to be deterred, the group took its fight to the Supreme Court. In its petition last October, it argued that it should not have to meet the typical standing requirements to bring a case in federal court because the AIA expressly gives it, and other third parties, the right to appeal the PTO's decision. Despite these arguments, the Supreme Court announced this February that it was declining to revisit the Federal Circuit's decision.

Consumer Watchdog's aggressiveness teaches an important lesson about the future of patent challenges on controversial technologies like stem cells. At first glance, Consumer Watchdog's fight against a patent that expires in 2015 would seem puzzling. The scientist-licensees that were named on the original reexamination challenges dropped off the case before the PTO's 2012 decision. These individuals, whether motivated by money or by an appeal to public fairness, were either satisfied that the reexaminations did the work of limiting Thomson's claims, settled with WARF privately, or simply felt it was time to move on. That left Consumer Watchdog with no real financial dog in the fight, other than an appeal to public policy.

But the concern with public access to promising technologies may motivate future attorneys to take up mantles against more stem cell patents, collaborating with publicly minded researchers as petitioners, just as with the *Myriad* case. In this way, the future of patent challenges may increasingly be at the hands of special interest, anti-patent groups and scientists, rather than spurned licensees.

Not all new stem cell patent disputes are so public-minded, however. As in the early days of the WARF challenge, the BioGatekeeper case appears to have those with financial interests challenging induced pluripotent stem cell (iPSC) patents. Currently an unknown entity, BioGatekeeper, Inc. filed an inter partes review against one of Nobel Prize winner Shinya Yamanaka's foundational iPSC patents. Like the Consumer Watchdog challenge, the BioGatekeeper challenge invokes obviousness: that the cellular reprogramming discovery was based on pre-existing art, publications, and patents that predate the Yamanaka filings (Simon et al., 2010). In this case, the prior art belongs to Rudolf Jaenisch,

the inventor and his employer, the Whitehead Institute.

Although the PTO ultimately declined to institute BioGatekeeper's challenge, the case stands as an example of how patent challenges become easier—and cheaper—to initiate after the passage of the AIA. There appear to be multiple motivations driving the low threshold use of the AIA. Analysts estimate that total global revenues for companies that supply iPSC research products will exceed $1 billion by 2015 (BioInformant Worldwide, 2014). The first clinical study involving the transplantation of iPSCs into humans began recruiting patients in August 2013. This safety study will use iPSC-derived retinal pigment epithelium to restore vision in patients with wet age-related macular degeneration, possibly addressing a large unmet medical need. The spoils of the market are being fought for among a highly fragmented group of dozens of patent holders, a third of which are corporate affiliated (Roberts et al., 2014). Thus, the AIA may provide a way for hungry market entrants to challenge patents on older, foundational research without the standing requirements present in the Consumer Watchdog suit.

The Future of Stem Cell Patents after the AIA

As the Consumer Watchdog and BioGatekeeper challenges illustrate, the AIA has provided broader avenues for third parties to challenge stem cell patents before the PTO. Although these procedures still possess limits, these cases do not appear to be isolated incidents. Rather, three facets of stem-cell-related patents in particular suggest that such exchanges are likely to become more frequent in the future.

First, there is good reason to believe that the robust licensing market that generated such peace among stem cell patent holders will not last forever. A recent study suggests that the biggest threat to the commercialization of iPSCs is "the potential formation of a patent thicket and mismanaged licensing practices in a field that has begun to privatize at an early preclinical phase" (Roberts et al., 2014). Given the rapid transfer of stem-cell patents from the public to the private sector, this threat is quite real. As such, the AIA seems to encourage commercial enterprises and inventors to file patent challenges early and often to stave off future competition or gain entry to the market.

Second, as stem cell biotech companies grow and become publicly traded, they increasingly become attractive targets for hedge funds seeking to take short positions. The AIA's new procedures allow short investors—as "non-interested parties"—to simultaneously challenge their target's patents at the PTO while taking a short equity position in the hopes of either profiting on the challenge's downturn or receiving a settlement payment. Indeed, this is precisely the strategy recently implemented by Dallas-based Hayman Capital in the pharmaceutical context. In February 2015, Hayman Capital filed its first inter partes challenge, against Acorda Therapeutics' patent on Ampyra, a multiple sclerosis drug (http://www.reuters.com/article/2015/01/07/pharmaceuticals-haymancapital-idUSL3N0UM42O20150107). As of April 2015, it has filed four more challenges. To the extent Hayman is successful, it may cause other stem-cell IP investors, like BioGatekeeper, to file additional challenges.

Lastly, the new system of inter partes review allows competing inventors and frustrated researchers a fast and cheap way to challenge patents—or to demand royalty-free licensing or academic credit. In addition, given the fractious history of stem cell research, groups that object to patenting on moral grounds—such as opposition to patenting forms of life—could deploy the AIA as a low-cost way to delay or derail the commercialization of new discoveries. Given the heated and very public priority disputes simmering in the stem cell field, this may remain more than a distant possibility in some extreme cases.

Whether the availability of new avenues to challenge patents means solutions or problems to stem cell patenting depends on the reader's point of view as to the propriety of stem cell patents in the first instance. As problems, the answer to fixing them lies in maintaining the robust licensing market that currently exists for many stem cell patents. As long as licensable patents are affordable, competitors will likely pay for certainty rather than a roll of the dice at the PTO. As solutions, time will tell whether the AIA ultimately has its intended effect of making it cheaper and easier to weed out bad patents before they wend their way into federal court.

Conclusions

Stem-cell-related patents have enjoyed a relatively stable existence since they began to be issued in the early 1990s. Much of that can be attributed to the robust licensing market for the underlying technologies and because few legal avenues existed for third parties to cheaply and effectively challenge overbroad or invalid stem cell patents. The AIA and the commercial development of new stem cell technologies may upset this balance. Although still constrained by limits—as demonstrated by the Consumer Watchdog and BioGatekeeper cases—new administrative procedures before the PTO make it substantially easier (and cheaper) to challenge stem cell patents as they become issued. This may be a natural stage in the life cycle of any rapidly developing area of law and technology.

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WEB RESOURCES

The URLs for data presented herein are as follows:

Trends From 2 Years Of AIA Post-Grant Proceedings, Law 360, http://www.law360.com/articles/581512/trends-from-2-years-of-aia-post-grant-proceedings

Inter Partes Review Initial Filings of Paramount Importance: What Is Clear After Two Years of Inter Partes Review Under the AIA, Mintz Levin Intellectual Property Advisory, http://www.mintz.com/newsletter/2014/Advisories/4363-1014-NAT-IP/.

Reuters, U.S. hedge fund plans to take on big pharma over patents, Jan. 7, 2015, http://www.reuters.com/article/2015/01/07/pharmaceuticals-haymancapital-idUSL3N0UM42O20150107.

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