ABSTRACT 1481

AMP V. MYRIAD GENETICS: GENE PATENTS, PATENTING LIFE, AND THE IMPACT ON US STEM CELL RESEARCH

Kirstin R.W. Matthews and Maude L. Cuchiara

Science and Technology Policy Program, Baker Institute, Rice University, Houston, TX

JAMES A. BAKER III INSTITUTE FOR PUBLIC POLICY
RICE UNIVERSITY

Introduction

In 1998 and 2000, Myriad Genetics was granted patents for two genes — BRCA1 and BRCA2 — which are implicated in hereditary breast and ovarian cancer (**see Figure 1**). Due to the patents, Myriad is currently the only company in the US that can conduct diagnostic testing for these genes. The patenting of the BRCA genes launched a raucous debate about the ability to patent life: **how do we distinguish between what is simply discovered and what is truly "made by man"?**

Here we will describe the progression of the ***Association for Molecular Pathology (AMP) v. Myriad Genetics*** case as well as compare the legal and scientific rationale for and against gene patents to that of human embryonic stem cell (hESC) patents. We will then discuss the arguments made by both sides to the US Supreme Court (US-SC) and speculate on how potential court rulings apply to the patenting of hESCs and surrounding technologies. We will also reflect on the appropriateness of these types of patents — comparing the BRCA gene and Wisconsin Alumni Research Foundation (WARF) stem cell patents.

History of Life Science Patents: Genes, Cells and Organisms

In 1980, the landmark case *Diamond v. Chakrabarty* guaranteed the ability to patent some forms of life. **The US-SC ruled that "anything under the sun made by man" was patentable.** This led to the patenting of transgenic mice strains (1988 "oncomouse"), hESCs (2001 WARF), and other living organisms or their components, including genes (**see Figure 2**). A biotechnology patent must meet the same criteria as other patents: 1) it must be novel; 2) it must be non-obvious to researchers in the field; and 3) it must have utility. In addition, the ruling identified three categories that are unpatentable: 1) laws of nature, 2) physical phenomena, and 3) abstract ideas.

The first patent for a gene was granted in 1982 for a gene fragment for the hormone endorphin. It is estimated that 20% of the human genome has already been patented in the US. **Patents have been granted for a variety of forms of DNA including cDNA, genes, and genetic diagnostics — although patents for entire genomes or human organisms are prohibited (Weldon Amendment).** The US Patent and Trademark Office (USPTO) states that "an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it."

In addition to patents for genes, patents for cells have been challenged recently. For hESCs, the majority of patents in the US are held by the Wisconsin Alumni Research Fund (WARF). In 2006, the Foundation for Taxpayer and Consumer Rights and the Public Patent Foundation asked the US Patent and Trademark Office (USPTO) to revoke WARF's patents. The USPTO ultimately validated the patents but limited their breadth.

Overview Of Myriad Court Case

The American Civil Liberties Union (ACLU) and the AMP challenged Myriad's gene patents in 2009 (**see Figures 1 and 2**). The US District Court (US-DC) invalidated the patents asserting that the process of isolating DNA does not fundamentally change the nature of DNA or the information on it and is thus unpatentable. But this ruling was challenged in US Federal Appeals Court (US-AC) and reversed in a 2-1 decision. AMP appealed this ruling to the US-SC. In 2012, the US-SC heard the case *Mayo Collaborative Services v. Prometheus Laboratories* and overturned a patent because the claims were a "law of nature." In light of this decision, the USPTO established new guidelines for evaluating patents and the US-SC returned *AMP v. Myriad Genetics* to US-AC which re-evaluated and upheld the patents.

On April 15, 2013, the US-SC finally heard arguments in the case. Overall, the court seemed determined to balance the economic incentives of patents with the preservation of research. **Many of the court's questions to both sides of the case revolved around the central idea of 'why the gene is or is not a product of nature.'** Hansen (counsel for AMP) argued that though important, the discovery of the BRCA genes was simply that—a discovery as opposed to a patentable invention. Castanias (counsel for Myriad Genetics) argued that the BRCA genes were indeed an invention because scientists created a new molecule; they decided where the gene began and ended in the genetic code.

During the hearing the patentability of cDNA was also discussed. Hansen was opposed to cDNA patents emphasizing that these fragments of DNA *did* exist in nature and were therefore, like genes, unpatentable. Castanias and Verrilli (the US Solicitor General) both agreed that cDNA is a manmade creation.

Sotomayor's final question to Hansen, "Is there some value to us striking down isolated DNA [patents] and upholding the cDNA [patents]?" might foreshadow the court's ultimate decision (see Figures 3 and 4). Based on the questions asked by the US-SC justices it appears that they might rule that genes themselves are not patentable but that cDNA that is created in a laboratory environment is. But the court could very well avoid addressing the issue entirely by ruling on a procedural issue. Regardless of the ruling, the decision will impact more than just gene patents, but potentially other biological patents including hESCs (**see Figures 3 and 4**).

Figure 1: Timeline of Myriad Genetics Court Case

1998

May 5
BRCA1 Patent US5747282A issued to Myriad Genetics. The gene was isolated in 1994 and the patent for it was filed in 1995. This patent covers three areas: 1) the isolation of the gene itself (composition); 2) the process of detecting the mutation (method); 3) the drug screening method to determine what therapeutics work best for certain mutations (drug screening).

2000

December 19
BRCA2 Patent US6162897A issued to Myriad Genetics. The gene was isolated in 1995 and the patent for it was filed in 1997.

2009

May 12
The Association for Molecular Pathology (AMP) filed a lawsuit against the US Patent and Trademark Office (USPTO) and Myriad Genetics stating the patents for BRCA1 and BRCA2 were invalid. The lawsuit was a result of Myriad's strict enforcement of their patents discouraging genetic testing services and academic research. In addition, AMP believed gene patents interfered with the practice of medicine and the ability of doctors to make treatment decisions.

2010

March 29
US District Court ruled that Myriad's patents were invalid. Judge Sweet ruled against all three claims: composition, method and drug screening. The isolation of the gene involved a law of nature, therefore unpatentable. The comparison of the DNA sequences in the method were abstract mental processes not a methodology and unpatentable. Finally, the drug screening involved cell growth rates which the judge decided was a basic scientific principle and not eligible to be patented either.

2011

July 29
US Appeals Court reversed District Court ruling and held that genes were eligible for patents. The Appeals Court overturned two of the rulings specifically on composition and drug screening. It determined that the gene is not found isolated in nature, therefore patentable. For the drug screening, the court believed that since the cells were transfected with the mutation, it was patentable. The judges did uphold the District Court's determination that the method was unpatentable.

December 7
American Civil Liberties Union (ACLU) filed petition for US Supreme Court review of the case.

2012

March 26
US Supreme Court vacated previous judgments and sent case to Appeals Court for review in light of recent Supreme Court ruling on *Mayo Collaborative Services v. Prometheus Laboratories*.

August 16
US Appeal Court ruled that the Myriad patents are legal. Similar decision as 2011.

November 30
US Supreme Court granted petition to review case.

2013

April 15
US Supreme Court heard arguments.

Summer
US Supreme Court will rule on case.

Figure 2: Timeline of US Life Science Patents and Laws

1980	*Diamond v. Chakrabarty*: "anything under the sun made by man" can be patented
1982	First gene patent granted, the hormone endorphin
1988	First animal patented, the "Oncomouse"
1998	BRCA1 gene patents issued to Myriad Genetics
2000	BRCA2 gene patents issued to Myriad Genetics
2001	hESC patents issued to WARF
2003	Weldon Amendment: patenting human organisms illegal
2006	WARF patents challenged. In 2010, USTPO invalidated one of WARF's patents (for hESC cultured without LIF) as "non-obvious" and others claims were narrowed.
2009	*AMP v. Myriad Genetics*: challenge of BRCA1/2 gene patents
2010	US Patent Reform Act: changed inventor from "first-to-discover" to "first-to-file"
2012	*Mayo Collaborative Services v. Prometheus Laboratories*: diagnostic test for drug dosing determined unpatentable
2013	Supreme Court hears and rules on *AMP v. Myriad Genetics*

Figure 3: Similarities and Differences Between Gene and hESC Patents and Their Court Discussions

Topic	*Gene Patents*	*hESC Patents*
Scientific Background	Both are isolated from a larger tissue.	
	Genes are taken from cells.	hESC are taken from blastocyst and grown in culture.
	Gene isolation does not require significant manipulation; the starting product is structurally similar to and encodes same information as final product.	hESC isolation requires a degree of manipulation—isolating cells then producing cell lines.
	DNA isolation is a standard procedure.	Cell isolation is a standard procedure, but there are novel procedures for cell growth.
Ethical and Moral Concerns	"Inventions" involve human components and as such some would consider patenting unethical.	
	Patents granted without considering ethical and moral implications.	
Claims	Both included composition and process claims.	
	Composition patents: genes, cDNA, mutated genes	**Composition patents:** hESC lines
	Process patents: Diagnostic test	**Process patents:** Growth/culture of cells
Opponents' Arguments	Patents' harsh licensing procedures stifle innovation and hinder progression of research.	
	"Inventions" did not meet criteria for patentability.	
	Gene is a product of nature and unpatentable.	Cells were an obvious discovery and unpatentable.
Supporters' Arguments	Patents are necessary to spur economic growth.	
	Both patents "made by man" because isolated forms not found in nature.	
Future of Patents	Some claims likely to be invalidated by Supreme Court.	Upheld by USPTO; May be challenged pending Supreme Court ruling on gene patents.

Figure 4: Outcomes of the Potential Supreme Court Rulings in *AMP v. Myriad Genetics*

Potential Rulings	Impact on Gene Patents	Impact on Bio Patents
All of Myriad's claims are valid.	Genes and cDNA are patentable.	Other biotech patents, including hESC patents, will stand, though these types of patents could be challenged for other reasons.
Genes are not patentable, but cDNA is patentable.	Distinguishes between genes and cDNA, ruling cDNA patentable because it has been manipulated by man.	Likely USPTO will issue new guidelines for bio patents. Since hESCs are also "isolated," USPTO would have to determine if processing after isolations is sufficient manipulation.
Neither genes nor cDNA are patentable, but the use of gene/DNA can be patented.	Genes and cDNA are unpatentable because they are a "law of nature."	Many bio patents including hESC patents will be reevaluated, specifically those involving "discovering" natural materials.
Neither genes and cDNA nor their use is patentable.	Confirms that genes and cDNA and their use are "laws of nature" and unpatentable.	Probable that hESC and other biological patents that could be considered "laws of nature" would be challenged in court and deemed unpatentable.
No ruling on claims.	Since no Supreme Court decision, gene patents would remain valid.	Encourage more descriptive laws regarding patents that involve "laws of nature."

Conclusions

When the US-SC rules on the validity of gene patents, it will have implications for all of biotechnology. At this point it is uncertain exactly how the court will rule, though the preeminent speculation is they will deem gene patents invalid while upholding patents for cDNA and other manipulated forms of genetic material. What is unclear is the rationale and language that the justices will use in their decision. This will be a major factor in how the ruling will affect other biological patents. Regardless, the ruling will spur debate on what should be patentable, what criteria should be used to evaluate patents, and who should conduct the evaluation.

By their own admission, the US-SC justices are not experts in any scientific field. They are being asked to rule on the validity of a patent when it is apparent that they do not completely comprehend the scientific principles and ideas that are being challenged. **Unfortunately the broadness of the *Diamond v. Chakrabarty* ruling — "anything under the sun made by man" can be patented — leaves it open for wide interpretation and has resulted in patent challenges in court despite the fact that these venues may not be the most appropriate for ruling on scientific material.**

It is our opinion that the rules for biotechnological patents should be revisited outside of a courtroom. Congress, with experts at the USPTO and in consultation with scientific and legal scholars, should discuss and evaluate the idea of patenting life and ultimately make the decision on patents instead of the courts. In fact, in the *AMP v. Myriad Genetics* case, all three US-AC judges interpreted the product of nature doctrine differently and used it to support their opinion.

Scientific discoveries are progressing forward, leading to innovation and new technologies. Inventors deserve patent protection, but the rights of patients and ethical implications should be considered before blindly granting them. Furthermore, the complexity of biotechnology might make the need for patents less important in the future. If it takes 20 years from "invention" to clinical use, how helpful is a patent if it has already expired by the time the treatment is approved?

Acknowledgements

We thank Shawn O'Neill for assistance with the poster development and design. This project was supported by the Baker Institute's Science and Technology Policy Program as well as the Baker Institute International Stem Cell Policy program which was endowed by the State of Qatar in collaboration with the Qatar Foundation for Education, Science and Community Development.

Further Information

For more information on this or related projects, please contact Kirstin Matthews at **krwm@rice.edu** or visit the Baker Institute Science and Technology Policy website at **www.science.bakerinstitute.org**. A PDF version of the poster is also available at **www.bakerinstitute.org/isscr2013-courts**. Follow us on Twitter **@stpolicy**.

Contact Information

The International Stem Cell Policy Program