The “Myriad” patent litigation Patentability of DNA molecules

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Overview

- A lawsuit by the American Civil Liberties Union, a well-known New York-based non-governmental civil rights organization
  - on behalf of several doctors who specialize in laboratory medicine, several breast cancer patients, genetic counselors, laboratory medicine organizations, and breast cancer patient advocacy groups.
- Against Myriad Genetics Inc., a company in Salt Lake City, Utah, that provides genetic testing services for determining the risk of hereditary breast and ovarian cancer in patients.*
- To invalidate claims in Myriad's patents to DNA molecules that relate to the BRCA1 and BRCA2 breast cancer genes.
- There are several laboratories in the U.S. that offer limited testing of these genes, but only Myriad provides full, comprehensive testing.
- The plaintiffs have said they want to break Myriad's monopoly for BRCA1 and BRCA2 testing.

* Myriad Genetics is not a member of BIO

Examples of challenged claims

- U.S. 5,747,282:

  1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.
  2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

- The challenged claims follow a 20 year-old standard format. This kind of claim is common in U.S. patents.
- An estimated 8,700 unexpired U.S. patents contain at least 1 claim of this type.
  - 40% relate to use in human medicine
  - 60% relate to other fields, such as veterinary medicine, agriculture, food and beverage manufacturing, industrial enzymes or bioenergy

Nature Biotechnology 31(5) (2013) 404-410.

What kind of lawsuit is this?

- Declaratory Judgment suit – a special kind of patent lawsuit where the patent owner is the defendant.
  - An "attack first" lawsuit by someone who has not been sued for patent infringement, but who feels harmed by the patent because, for example, they would likely be sued.
  - Requires an actual, underlying legal dispute between the parties. Not like nullity or revocation lawsuits in some countries.
- Summary Judgment – the case was first decided under an abbreviated procedure requiring no examination of witnesses and limited facts.
- Such lawsuits are sometimes difficult for the courts because they can be somewhat abstract and hypothetical. There may be no actual infringing activity to which the claims can be compared. The courts have less information than in an infringement lawsuit.

Procedural history

- March 29, 2010: U.S. District Court for the Southern District of New York holds claims invalid under Section 101 of the U.S. Patent Act
- July 29, 2011: U.S. Court of Appeals for the Federal Circuit reverses the lower court * Three judges write 3 separate opinions.
- March 26, 2012: U.S. Supreme Court vacates the decision and remands for reconsideration in light of *Mayo v. Prometheus* 132 S.Ct. 1289
- August 16, 2012: U.S. Court of Appeals for the Federal Circuit again reverses the lower court's decision. Again 3 judges write 3 opinions.
- November 30, 2012: U.S. Supreme Court grants review.

* The lower court had also struck down certain Myriad patent claims to broad and generalized methods of comparing BRCA DNA sequences. The invalidation of these method claims was affirmed by the appellate court and is not discussed in this presentation.

Legal theories (1)

- The question is NOT novelty; unobviousness/inventive step; sufficiency of technical disclosure; or utility/industrial applicability.
- Patent-eligible subject matter: *"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof… subject to the conditions and requirements of [the Patent Act]"* 35 USC 101.
- Suggests that courts should ask: "is the patent claim directed to something that was 'composed' or 'manufactured' or 'improved' by man?"
- For example:
  - "a new mineral found in the earth" was not 'composed' by man; or "a new plant found in the wild" was not 'manufactured' by man – neither would be patentable. *Diamond v. Chakrabarty* 447 U.S. 303 (1980)
  - "A *signal* with embedded supplemental data" is not patentable because a "signal" is not a process; a machine; a manufactured article; or a composition of matter. *In re Nuijten* 500 F.3d 1346 (Fed. Cir, 2007).

Legal theories (2)

- But: historically, the U.S. Supreme Court has sometimes applied rules from its own earlier cases, even if they're not part of the "conditions and requirements" of the Patent Act.
- Under U.S. Supreme Court law, "laws of nature, physical phenomena, or abstract ideas" are excluded from patentable subject matter.
- The Supreme Court has applied and developed this exception for "manifestations of nature" in at least 5 cases between 1972 and 2012. These cases dealt with processes involving mathematical or logical operations.
- Two of these cases were decided after the Myriad litigation started.
- The Supreme Court's exceptions have generated a large amount of legal commentary, and many different opinions on how they should be practically applied. (e.g. *CLS Bank v. Alice*, (Fed. Cir. May 10, 2013) (Seven different opinions by 10 judges).

Arguments against patent-eligibility

- The challengers say that isolated DNA molecules should fall under the exception for natural phenomena because genes exist in nature.
- Isolated DNA molecules having natural sequences are not sufficiently different from natural genes.
- They have only been removed from their natural environment, but they're still the same.
- The patentee hasn't made them more useful.
- The patentee has only discovered them, not invented them.
- The "isolated DNA claims" interfere with scientific progress, because they prevent anyone from studying or using the natural gene.

Arguments for patent-eligibility

- The defenders say that isolated DNA molecules are not a natural phenomenon because:
- The patents don’t claim anything in anyone’s body.
- Isolated DNA molecules are obtained in the laboratory and do not exist in nature.
- They are chemically quite different from natural genes.
- They are useful for new technical applications that are not possible with natural genes.
- They required great technical and intellectual effort by scientists in order to become known and available for human use.

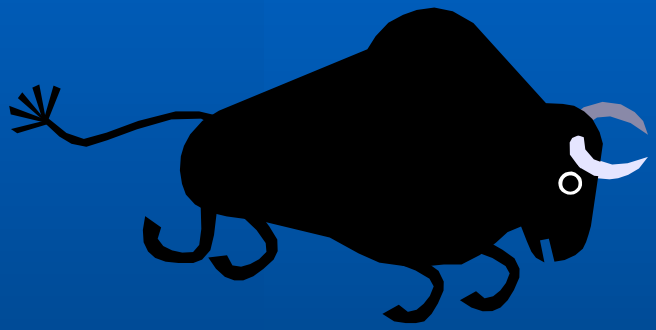
Remarks

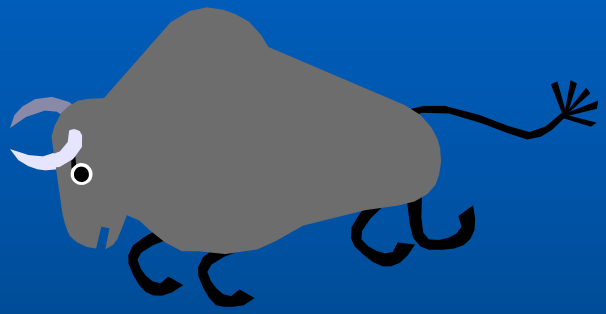
- The questions that need to be answered depend on many technical facts. They cannot be answered by just arguing about the law. For example:
  - "How different is the claimed isolated DNA molecule from a natural gene?"
  - "Would the patent claims always be infringed if someone did research on the natural gene?"
  - "Does the claimed isolated DNA actually exist in nature?"
- In the U.S., the technical facts in a lawsuit are established in the lower court (district court). No new facts can be added in the higher courts.
- After the district court decided the *Myriad* case, the U.S. Supreme Court decided 2 other cases in this area of the law [*Bilski v. Kappos* (2010) and *Mayo v. Prometheus* (2012)].
- These cases influenced the legal questions about the *Myriad* case in the higher courts, but no new technical facts could be added to answer them, thereby increasing confusion and disagreement during the appeals.

Remarks (2)

- The *Myriad* case involves a very broad legal question: Should an isolated DNA molecule be excluded from patentability, even if it was not known before, has been isolated from nature for the first time, and its structure and form is clearly characterized, and has practical value in industry?
- Because of this broad legal question, the U.S. Supreme Court may find it very hard to limit its decision to only Myriad's patents. Its decision could affect many other patents:
  - If claims to isolated BRCA DNA are not patentable, claims to other isolated human DNA would also not be patentable;
  - If claims to isolated human DNAs are not patentable, claims to isolated animal, plant, or microbial DNA would also not be patentable.
  - If claims to isolated DNA are not patentable, why would claims to other isolated molecules be patentable? For example medicinal substances that are isolated from plants?

What about the public interest?





"Patients don't have access"
"Patents increase prices"
"Patents interfere with research and medical care"
"Myriad is a bad company"
"What the other side is saying is not true"

"Patents are needed for business investment"
"Patents create new and better products"
"Patents create new businesses and jobs"
"Myriad is a good company."
"What the other side is saying is not true"

What about the public interest? (2)

- Policy questions affect everyone. They cannot be decided in a lawsuit between only two parties.
- That's why judges rely on the law, not on policy, to decide whether a patent is valid or not.
- For example:
  - If a patent owner is a "bad actor," that doesn't mean his patent is invalid.
  - If a consumer cannot get access to the patented product, that doesn't mean the patent is invalid.
- But: The public interest is important . There is a tendency in U.S. patent law to preserve the public interest without destroying the patent right altogether. In fact, patent rights are also in the public interest, and must be balanced against other public interests.

What about the public interest? (3)

- For example: In 1995, Congress determined that it would be against the public interest if medical doctors could be sued for patent infringement for practicing surgery.
- It was first proposed to forbid all patents for doing surgical procedures and administering medical therapies. But Congress decided to not ban such patents. Instead, medical doctors were given immunity for certain patent-infringing medical activities. 35 USC 287(c) (1996). This balanced the public interests without destroying patents altogether.
- For example: In the 1930s the City of Milwaukee operated a sewage treatment facility that used a patented process for treating waste water. Even though there was an extraordinary public interest, the court found that the patent was both valid and infringed. The court decided that the patent owner should be compensated financially, but that the plant should not be shut down. *Milwaukee v. Activated Sludge* 69 F.2d 577

Public interest example: Amgen v. Roche

- Example: In *Amgen v. Roche* 581 F. Supp. 2d 160 (D. Mass 2008), after patents were found valid and infringed, the patent owner sought an injunction to block a competing drug from entering the market.
- Under U.S. patent law, a patent owner seeking such an order must prove
  - (1) that it would suffer an irreparable injury;
  - (2) that money payments would not be sufficient to compensate for the injury;
  - (3) that the balance of fairness and harm to both parties favors the patentee; and
  - (4) that the public interest would not be disserved by a permanent injunction.
- The judge considered factors 1-3 in favor of the patent owner - but the main focus was on the public interest. The judge appointed a special master and a technical expert and held 4 days of hearings to balance the public interest factors of: (i) patient health; (ii) medical cost savings and (iii) patent-based incentives for innovation.

Public interest example: Amgen v. Roche (2)

- Patient health: do existing treatments meet the medical needs of patients? The judge found that patients and doctors would probably benefit from additional choice. But it was not clear that the infringing drug would provide significant clinical advantages over existing treatments.
- Medical cost savings: The judge found that market entry of the infringing drug would not necessarily result in overall lower cost to public payors. Also, just because an infringing product is cheaper is not a good reason: A copied product can always be sold cheaper than the original.
- Innovation: The judge stated that the breakthrough innovation was made by the patent owner, and that the infringing drug was “just” an improvement of the patent owner’s existing drug. The public interest in breakthrough innovations is stronger than the public interest in small improvements. Drug innovation is very time-consuming, risky, and expensive, and strong patent rights are a very important incentive.

Public interest example: Amgen v. Roche (3)

- The *Amgen* case teaches us that public interest considerations get very complicated very quickly, and that a lot of facts must be considered in order to make a reliable, evidence-based decision.

- The judge in the *Amgen* case wrote that he at first wanted to allow the infringing drug on the market. But after he had considered all the facts, he reached a different conclusion.
- In the *Amgen* case, the judge appointed a neutral expert to explain the technical questions. He also appointed a special master (an officer of the court to manage especially complicated and difficult issues), and heard evidence during four full days of testimony.
- In comparison, the judge in the *Myriad* case held a single two hour hearing on summary judgment motions.

Do patents interfere with basic research?

- The popular press is saying that patented things cannot be further researched by others.
- This theory is presented to support section 101 ineligibility even by some departments of the U.S. Government: important discoveries should be excluded from patenting, because scientists and researchers must be free to work on them.
- *"Myriad and other gene patent holders have gained the right to exclude the rest of the scientific community from examining the naturally occurring genes of every person in the United States"* [1]
- *"Any scientist who wants to conduct research on such a gene - even on a small sequence of its DNA - has to pay license fees."* [2]
- Such statements are often repeated in U.S. newspapers. However, they are not true

[1] Adam Liptak, *Supreme Court to Look at a Gene Issue,* N.Y. Times, Nov. 30, 2012
[2] Michael Specter, *Can We Patent Life?,* The New Yorker, April 2, 2013

Do patents interfere with basic research? (2)

- The question whether patents interfere with basic research has been studied repeatedly. The National Academies, the American Association for the Advancement of Science, the Federal Trade Commission, and academic scholars have concluded that there is little evidence that patents prevent scientists from doing research on patented inventions.
- For example, the BRCA genes are among the most heavily studied human genes. More than 5,000 scientific papers have been published since 1998 by thousands of researchers without patent licenses.
- The U.S. Patent Act does not have an explicit exception for basic experimentation. But it is a very old principle that someone "who constructed a [patented] machine merely for [scientific] experiments or for the purpose of ascertaining the sufficiency of the machine to produce its described effects" would not be held liable. *Whittemore v. Cutter* 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813).

Do patents interfere with basic research? (3)

- It is clear that there is an exception for scientific experimentation in U.S. patent law, but it is unclear how broad it is. Because there are no lawsuits about this question, judges have had almost no opportunity to make the law clearer.
- Judge Newman of the U.S. Court of Appeals for the Federal Circuit provided an analysis according to which the following would not be patent infringement under the "experimental use" exception*:
  - Experiments to understand how a patented invention works, and to verify whether it does what the patentee says it does;
  - Experiments to improve a patented invention;
  - Experiments to determine whether a patented invention can be used in new ways;
  - Experiments to compare a patented invention with alternatives.

* *CLS Bank v Alice Corp*., 2011-1301, slip op., Fed Cir. May 10, 2013, Newman, J., concurring/dissenting in part

Who should decide this question?

- There are three sources of patent policy in the U.S.: The USPTO, the courts, and Congress. Which one is best equipped to decide whether isolated DNA molecules should be excluded from the patent system?
- The USPTO: Has strong technical expertise. It receives input on regulations and guidelines through public notice-and-comment procedures. The USPTO must consider public comments and explain its conclusions and decisions. It can make limited policy, but is restricted by the patent statute and higher court decisions. The USPTO is best equipped to answer complicated technical questions that can be decided within existing law.
  - For example, between 1999 and 2000 the USPTO went through a public comment process for DNA patents. In its final guidelines, the USPTO determined that patents on isolated DNA molecules do not claim a natural phenomenon, and can be permissible under patent law. However, the USPTO raised the standard by requiring such patents to disclose a “specific, substantial, and credible utility.” Thousands of patent applications were subsequently rejected under this standard.

Who should decide this question? (2)

- The courts: The courts have non-specialist judges. Almost none have a scientific or technical education. The courts decide particular disputes between two or more parties.
- They are limited by the way the parties to a lawsuit define their dispute, and by the information and legal theories the parties put in the case.
- The courts can receive public comments through “amicus briefs” but don’t have to consider them.
- The courts are equipped to decide particular disputes as defined by the parties, not to create “the best solution for everyone.”
- Decisions can sometimes affect many other patent owners who are not part of the lawsuit, and result in “policy.”

Who should decide this question (3)

- The Congress: Non-specialist legislators from a range of professional backgrounds. Congress receives wide input from other parts of the Federal Government, state governments, and many public stakeholders. Any member of the public can petition and be heard. Congress can collect large amounts of facts to make decisions. It can change the law to craft "the best solution for everybody."
  - For example: In 1984, Bolar Pharmaceutical Co. argued to the U.S. Court of Appeals for the Federal Circuit that an exception to patent infringement should be created to resolve a conflict between the patent laws and the food and drug laws. But the court replied that only Congress, not the court, has the ability to "maximize public welfare through legislation." 733 F.2d 858 (1984).
  - Later that year, Congress passed the Hatch-Waxman Act, which created a special infringement exception, but it also compensated patent holders with additional patent term restoration. The USPTO or the courts could not have created such a solution.

What could this case mean?

- It is too soon to tell. The Supreme Court may be looking for a way to decide this case on narrow grounds. But it could be difficult to decide this case without affecting many other patents.
- The *Myriad* case is not just about Myriad's patents. It's about a whole category of patents. If patents on isolated BRCA DNA molecules are invalid because human BRCA genes exist naturally, then:
  - How can patents on other isolated DNA molecules with human sequences be valid?
  - How can patents on isolated DNA with animal, plant, or bacterial sequences be valid?
  - How can patents on other isolated substances from natural sources be valid, e.g. pharmaceutical substances from plants, antibiotics from fungi, enzymes from bacteria?
- The majority of companies that own such patents work on medicines, agriculture, bioenergy, or industrial biotechnology. Very few provide diagnostic testing services.
- This case focuses only on the behavior of a single company, but many other companies would be affected.

What could this case mean? (2)

- It is difficult to predict what this case could mean for patients or medical care. Myriad has hundreds of other patent claims that are not in this case. Even if the Supreme Court decides in favor of the ACLU, there will not be complete freedom-to-operate.
- It is unlikely that the prices for diagnostic testing will generally decrease. Researchers have found that the price of genetic tests depends not on patents, but on how complicated the test is, and on the reimbursement rates set by insurance companies.
- The cost or BRCA testing is around $3,800 – approximately the cost of an MRI scan. Health insurance companies already widely pay for BRCA testing.
- But insurance companies will only pay if the test is medically necessary according to their medical guidelines. This is normally the reason why a patient cannot have the test.

Thank you!

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