Isolated human genes and related therapeutic treatment methods held patent-eligible

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Ass'n for Molecular Pathology v US Patent & Trademark Office, 689 F 3d 1303, Fed Cir ('Myriad IV'), 16 August 2012

Patents on isolated genes are big business. In the past three decades, the United States Patent and Trademark Office (USPTO) has issued over 2500 patents claiming isolated DNA, and 40000 DNA-related patents in nonnative form, for genes in the human genome. Thus in 2010, when a US district court judge found claims to isolated DNA and related method claims patent-ineligible, the industry was shocked and mobilized to respond: see *Ass'n for Molecular Pathology v US Patent & Trademark Office*, 702 F Supp 2d 181, 220–37 (SDNY 2010) ('*Myriad I*'). At first, on appeal, the majority of a three-judge panel of the US Court of Appeals for the Federal Circuit reversed the district court decision and found all of the composition claims, as well as one method claim directed to screening potential cancer therapies based upon changes in the growth rates of transformed cells, patent-eligible: *Ass'n for Molecular Pathology v US Patent & Trademark Office*, 653 F 3d 1329 (Fed Cir 2011) ('*Myriad II*'). This result was shortlived: the US Supreme Court, in *Mayo Collaborative Services v Prometheus Laboratories, Inc*, 132 S Ct 1289 (2012) ('*Mayo*'), granted certiorari, vacated *Myriad II* and remanded for further consideration in view of *Mayo*. *Ass'n for Molecular Pathology v Myriad Genetics, Inc*, 132 S Ct 1794 (2012) ('*Myriad III*'). This past August, in *Myriad IV*, the Federal Circuit, on remand, quickly set a new briefing schedule to address the impact of *Mayo* on its prior *Myriad II* decision, held oral argument, and then the same panellists reissued a substantively similar decision. While each of the panellists considered *Mayo*, it had little impact on their ultimate conclusions as to whether isolated DNA claims and related method claims were patent-eligible.

Legal context

Under the Patent Act, '[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title' (35 USC §101). Relying upon Congressional intent and a long history of judicial construction, the Supreme Court has made clear that the statutory categories of patent-eligible subject matter, ie processes, machines, manufactures and

compositions of matter, are to be broadly construed to include 'anything under the sun that is made by man': see eg *Diamond v Chakrabarty*, 447 US 303, 308 (1980).

However, the US Supreme Court has also 'undoubtedly recognized limits to §101 and every discovery is not embraced within the statutory terms'. Laws of nature, natural phenomena, and abstract ideas are excluded from patent protection: *Diamond v Diehr*, 450 US 175, 185 (1981).

In the wake of *Chakrabarty*, which recognized that 'a live, human-made micro-organism' is patentable subject matter, the US Patent and Trademark Office (USPTO) issued a large number of patents relating to DNA molecules for almost thirty years. It is estimated that there are 40000 US patents broadly related to human genes (Eric J Rogers, *Can You Patent Genes? Yes and No*, 93 J Pat & Trademark Off Soc'y 19, 40 (2010)). This genetic material has been found to be patentable, partly because isolated DNA is not found in nature. Rather, isolated DNA is the product of the chemical manipulation of genes, ie the excision, splicing or alteration of selected portions of natural genetic material. Therefore, isolated DNA has been considered patent-eligible under US law as a composition of matter. While the patenting of genetic material has been legally long settled, it has remained politically controversial, particularly in view of *Myriad I*.

In 2009, a number of medical associations, doctors and patients challenged the patent eligibility of claims in seven patents held in part by Myriad Genetics and the University of Utah Research Foundation ('Myriad'). In a surprising decision, at the trial court level on summary judgment, Judge Sweet found all of the claims to be patent-ineligible: *Myriad I*, 702 F Supp 2d at 220–37.

On appeal, a split three-judge panel of the Federal Circuit in *Myriad II* reversed in part, finding all of the composition claims, as well as one method claim directed to screening potential cancer therapies based upon changes in the growth rates of transformed cells, to be patent-eligible: *Myriad II*, 653 F 3d at 1329. Each US Circuit Judge on the panel, Judges Lourie, Bryson and Moore, penned their own opinions.

Thereafter, a petition for certiorari was filed with the US Supreme Court, taking issue with *Myriad II*'s holding of patent-eligibility. While that petition was pending, the US Supreme Court took up the issue of patent eligibility and issued its seminal decision in *Mayo* . In *Mayo*, the court invalidated certain blood testing method claims directed towards diagnosing and treating a disease under 35 USC §101 for claiming patent-ineligible 'laws of nature'. In response to the petition on *Myriad II*, the US Supreme Court issued a summary order granting certiorari, vacating *Myriad II* and remanding the case to the Federal Circuit to be reconsidered in light of *Mayo*: *Myriad III*, 132 S Ct 1794 (2012). On remand, the Federal Circuit quickly issued an order calling for a briefing schedule on the impact of *Mayo* on its prior panel decision regarding the patent-eligibility of certain claims, held a prompt oral argument, and, in August 2012, issued *Myriad IV*.

Facts

The district court action and decision

In 2009, a number of medical associations, doctors and patients, represented by the American Civil Liberties Union and the Public Patent Foundation, challenged the patent eligibility under 35 USC §101 of fifteen claims from seven patents held in part by Myriad. These patents—US Patents Nos 5,747,282 ('the '282 patent'); 5,837,492; 5,693,473; 5,709,999 ('the '999 patent); 5,710,001 ('the '001 patent'); 5,753,441; and 6,033,857— relate to the diagnosis and treatment of cancer in human beings. They include three types of challenged claims:

1. composition claims directed to isolated DNA molecules (eg the '282 patent, claim 1);
2. method claims directed to identifying cancer-predisposing mutations by analysing or comparing a patient's DNA sequence to a normal sequence (eg the '001 patent, claim 1); and
3. a method claim directed to screening potential cancer therapies based upon changes in the growth rates of transformed cells (eg the '282 patent, claim 20).

On summary judgment at the trial court level, Judge Robert Sweet of the US District Court for the Southern District of New York held that all fifteen claims at issue were drawn to non-patentable subject matter and were therefore invalid under 35 USC §101: *Myriad* I, 702 F Supp 2d at 220–37.

1. The first category of claims, the composition claims, relate to two specific isolated human genes, BRCA1 and BRCA2, and various mutations in those genes associated with breast and ovarian cancer. Claim 1 of the '282 patent is a representative composition claim:

   An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2. Judge Sweet found the composition claims were patentineligible, reasoning that the claimed isolated DNA molecules were not 'markedly different' from native DNA and therefore fell within the 'products of nature' exception to §101: *Myriad I*, 702 F Supp 2d at 220–32.
2. The second category of claims, including all but one of the method claims at issue, are directed to identifying cancer-predisposing mutations by analysing or comparing a patient's DNA sequence to a normal sequence. Claim 1 of the '001 patent is representative of these method claims:

   A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises. . . comparing a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene,

BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample. With respect to these claims, Judge Sweet found that the method claims directed to identifying cancer-predisposing mutations by analysing or comparing a patient's DNA sequence to a normal sequence were also patent-ineligible, because they failed the then-definitive 'machine-or-transformation' test. In particular, he found that these claims were ineligible for patent protection because they covered mental processes that were independent of any physical transformation: *Myriad I*, 702 F Supp 2d at 233–36.

3. The last method claim at issue involves a method of screening potential cancer therapies. Claim 20 of the '282 patent reads:

   A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic. With respect to this method claim, Judge Sweet found that the method claim directed to screening potential cancer therapies based upon changes in the growth rates of transformed cells was also patent ineligible because it covered a basic scientific principle. He concluded that any transformative steps were simply preparatory data gathering: *Myriad I*, 702 F Supp 2d at 237.

The appeal and first Federal Circuit panel decisions

Myriad appealed the district court's decision to the Federal Circuit.

In July 2011, in a split decision, a three judge panel of the Federal Circuit reversed in part, finding the composition claims at issue to be patent-eligible, but agreeing that the method claims relating to analysing or comparing certain DNA sequences were patent-ineligible on the ground that they claim only abstract mental processes: *Myriad II*, 653 F 3d at 1333–34. Judge Lourie wrote for the majority.

As to the method claim relating to screening cancer therapies based upon changes in cell growth rates, the Federal Circuit found this claim to be patent-eligible, because in addition to the comparing and analysing steps, it also recited the steps of growing transformed cells and determining those growth rates. The Federal Circuit concluded that these steps were transformative, not merely preparatory, and that therefore this claim was patent-eligible.

In a separate opinion Judge Moore, in *Myriad II*, concurred in part with Judge Lourie's majority opinion. First, she joined the majority opinion with respect to standing and the patentability of

the method claims at issue. However, since she believed that claims directed to isolated DNA sequences presented a different set of issues, she joined the majority with respect to claims to isolated cDNA sequences and concurred in the judgment with respect to the remaining sequences, for which she offered her separate reasoning.

In another separate opinion, Judge Bryson concurred in part and dissented in part. More particularly, he concurred with the portions of this court's judgment that were directed to the patentability of the cDNA claims and the patentability of the method claims. However, he dissented from the court's holding that Myriad's BRCA gene claims, and its claims to gene fragments, were patent-eligible. In particular, Judge Bryson explained (at 1373):

In my view, those claims are not directed to patentable subject matter, and if sustained the court's decision will likely have broad consequences, such as preempting methods for whole genome sequencing, even though Myriad's contribution to the field is not remotely consonant with such effects.

The Supreme Court GVR

Shortly thereafter, the Supreme Court granted certiorari, vacated *Myriad II* and remanded the case to the Federal Circuit to be reconsidered in light of its recent decision in i, which related to patent-eligibility. In *Mayo*, the Supreme Court had invalidated certain blood testing method claims directed towards diagnosing and treating a disease for claiming unpatentable laws of nature.

Analysis

In their decisions on remand, the three judges of the same panel at the Federal Circuit largely followed their prior opinions in *Myriad II*, with Judge Lourie for the majority noting that '[t]he principal claims of the patents before us . . . relate to isolated DNA molecules' and that 'Mayo does not control the question of patent-eligibility of such claims:' *Myriad IV*, 689 F 3d at 1325. The Federal Circuit panel decisions was unanimous with respect to the method claims. However, there were differences of opinion between the judges as to the patent-eligibility of the composition claims. Each member of the panel again wrote a separate opinion.

Judge Lourie's majority decision

In the majority opinion, written by Judge Lourie, the court framed the legal issue on the patent eligibility of the composite claims as whether and to what degree isolated DNA molecules fall within the exception for products of nature.

Judge Lourie found useful guidance from the two leading US Supreme Court decisions on the natural phenomena exception to patent eligibility: *Chakrabarty* (holding a

man-made microorganism patent eligible, even though it was 'alive') and *Funk Brothers Seed Co v Kalo Inoculant Co*, 333 US 127 (1948) (finding a mix on natural occurring bacteria not patent-eligible).

In *Funk Brothers*, the US Supreme Court found a mix of nitrogen-fixing bacterial cultures that inoculated a broader range of leguminous plants than single-species cultures to be patent-ineligible: since no species acquired a different property or use, applying the newly discovered bacterial compatibility to create a mixed culture merely amounted to merely taking advantage of the 'work of nature', and was not a patent-eligible advance.

By contrast, in the later *Chakrabarty* decision, the US Supreme Court addressed found a man-made microorganism designed to break down crude oil was a patenteligible 'composition of matter'. Although the microorganisms were genetically engineered with various naturally occurring DNA plasmids, the court found them to be patent-eligible because they were 'not . . . a hitherto unknown natural phenomenon, but . . . a nonnaturally occurring . . . composition of matter—a product of human ingenuity "having a distinctive name, character [and] use"': 447 US at, 309–10.

From his analysis of *Chakrabarty* and *Funk Brothers*, Judge Lourie divined that one way to distinguish 'between products of nature and human-made invention for purposes of § 101 turns on a change in the claimed composition's identity compared with what exists in nature': *Myriad IV*, 689 F 3d at 1327–28.

With respect to the Myriad isolated DNA claim, Judge Lourie reasoned the isolated DNA in the composition claims was a 'free-standing portion of a larger, natural DNA molecule' that has been chemically severed and manipulated:

BRCA1 and BRCA2 in their isolated states are different molecules from DNA that exists in the body; isolated DNA results from human intervention to cleave or synthesize a discrete portion of a native chromosomal DNA, imparting on that isolated DNA a distinctive chemical identity as compared to native DNA. Thus the challenged claims were drawn to patent-eligible subject matter, because the claims cover molecules that are markedly different—have a distinctive chemical structure and identity—from those found in nature. Judge Lourie rejected the plaintiffs' contention that the native and isolated DNA molecules were the same because they contained the same nucleotide sequence, holding:

[T]he patent-eligibility of an isolated DNA is not negated because it has similar informational properties to a different, more complex natural material. The claimed isolated DNA molecules are distinct from their natural existence as portions of larger entities, and their informational content is irrelevant to that fact.

Since the claimed isolated DNA molecules did not fall within the 'product of nature' exception, the claims were patent-eligible.

Significantly, Judge Lourie declined the invitation to make patent policy noting that '[w]hether its unusual status as a chemical entity that conveys genetic information warrants singular treatment under the patent laws . . . is a policy question that we are not entitled to address' ibid, 1330.

Turning to the method claims directed to identifying cancer-predisposing mutations by analysing or comparing a patient's DNA sequence to a normal sequence, the majority once again found, as it had in *Myriad II*, these claims to be patent-ineligible because they included no transformative steps and were directed to abstract mental processes. As stated, these claims:

[R]ecite[] nothing more than the abstract mental steps necessary to compare two different nucleotide sequences . . . Although the application of a formula or abstract idea in a process may describe patent-eligible subject matter, Myriad's claims do not apply the step of comparing two nucleotide sequences in a process. Rather, the step of comparing two DNA sequences is the entire process that is claimed (ibid, 1334–35, citation omitted).

Accordingly, these claims were found to be indistinguishable from the claims struck down by the Supreme Court in *Mayo*, and thus patent-ineligible under 35 USC §101. Finally, however, claim 20 of the '282 patent, the method claim directed to screening potential cancer therapies based upon changes in the growth rates of transformed cells, was found to be patent-eligible. *Myriad II* had previously come to the same conclusion based on the fact that the claim required certain transformative steps. This analysis was revisited in light of *Mayo*, which held that certain transformative steps are not necessarily sufficient under § 101 if the recited steps only relied on natural laws.

Judge Lourie in *Myriad IV* again concluded that this method claim was patent-eligible, because it recites a screening method based on the use of transformed, nonnaturally occurring cells, and therefore the claim 'includes more than the abstract mental step of looking at two numbers and "comparing" two host cells' growth rates'. Significantly, he found that once it has been determined that a new composition of matter is patent-eligible, 'applying various known types of procedures to it is *not* merely applying conventional steps to a law of nature': ibid, 1336 (emphasis added). Thus, the fact 'that the claim also includes the steps of determining the cells' growth rates and comparing growth rates does not change the fact that the claim is based on a man-made, non-naturally occurring transformed cell—patent-eligible subject matter'. In other words, *Mayo's* analysis regarding 'applying various known type of procedure' does not apply because modified DNA is not a product of nature.

Judge Moore's concurring opinion

Judge Moore concurred in part with the majority opinion's conclusion that the composition claim was patent eligible, but wrote separately to express different reasoning and some more specific concerns regarding claims to longer strands of isolated DNA.

Judge Moore's particular concern was not directed towards claims covering the shorter and more obviously manipulated DNA molecules (cDNA): 'It is not the chemical change alone, but that change combined with the different and beneficial utility [as diagnostic tools] that leads me to conclude that small isolated DNA fragments are patentable subject matter.' However, 'the longer strands of isolated DNA . . . which include most or all of the gene present a more difficult case' because the longer strands of isolated DNA 'do . . . not clearly have a new utility and appear[] to simply serve the same ends devised by nature.'

Despite this concern, Judge Moore nevertheless held the 'long strand' composition claims were patent-eligible based on the traditionally expansive scope of patentable subject matter, the PTO's long-standing policy of allowing patents on isolated DNA, and the settled expectations of the biotech industry.

Judge Bryson's dissent

Judge Bryson, on the other hand, penned a heated dissent regarding the patent-eligibility of Myriad's composition claims. Framing the question as 'whether the process of isolating genetic material from a human DNA molecule makes the isolated genetic material a patentable invention', he concluded that it did not.

Reasoning that '[t]he only material change made to those [isolated] genes from their natural state is the change that is necessarily incidental to the extraction of the genes from the environment in which they are found in nature', Judge Bryson concluded this meant they 'fall clearly on the "unpatentable" side of the line the [Supreme] Court drew in *Chakrabarty*'.

He further explained that even if the isolated DNA molecules had a different use from their natural one, they would not be patent-eligible since the key to their utility is that 'each gene must function in the same manner in the laboratory as it does in the human body . . . The naturally occurring genetic material thus has not been altered in a way that would matter . . . : ibid, 1350, 1354.

He concluded by criticizing the majority and concurring opinions for their reliance on USPTO policy, since that office has no law-making power, and on the settled expectations of the biotech industry, since there was no collective right to adverse possession to intellectual property.

Practical significance

Myriad IV reveals an effort by the panellists to diminish the impact of *Mayo* on the Federal Circuit's patent-eligibility analysis. By reaching the same conclusions on remand in *Myriad IV* that the panellists had previously reached in *Myriad II*, with only minor changes in the reasoning, it seems that the Supreme Court's mandate to

reconsider its prior rulings in light of *Mayo* had little impact.

Given the history of this case and the on-going consideration of patent-eligibility by the courts, it is doubtful that *Myriad IV* will be the last word on patent-eligibility of isolated DNA, or even the *Myriad* claims.

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