

Pigs Return to Earth: Federal Circuit Reinstates Most—But Not All—of Myriad’s Patents

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The Federal Circuit’s [long-awaited decision](#) (pdf) in *Association for Molecular Pathology v. USPTO* (the [Myriad gene patent litigation](#)) was issued this past Friday. As we were writing, with the economy having slowed to a barely perceptible crawl and a government default looming more likely by the hour, there were plenty of reasons to believe that the sky was falling. But the *Myriad* decision was not, and is not, one of them.

For the most part, the Federal Circuit’s 2-1 decision returned the law to the state it was in before [District Judge Sweet’s opinion turned things upside-down](#) last March. Although full of interesting rhetoric, the court’s three lengthy opinions (a total of 105 pages) are less remarkable for what they decide than for what they invite higher authorities—the Supreme Court and the Congress—to decide down the road.

First, the scorecard. The court’s *judgment*—that is, the holding, or outcome—was joined by Judges Lourie and Moore. A third member of the panel, Judge Bryson, dissented in part, meaning that he joined only a portion of the judgment (more on that below) and disagreed with another part.

The majority held as follows:

1. On the threshold procedural question of standing, the district court’s ruling was *affirmed*, with one plaintiff (Dr. Harry Ostrer) having sufficient standing to challenge Myriad’s patent claims.
2. Isolated genes, cDNAs and partial isolated gene sequences are patentable subject matter under § 101 of the Patent Act. Consequently, the district court’s judgment invalidating all of Myriad’s *product* claims to BRCA genes and fragments was *reversed* in its entirety.
3. Myriad’s claims to *methods* of screening potential cancer therapeutics by analyzing growth rates of cells with altered BRCA genes in the presence or absence of the treatments were also held to be directed to patentable subject matter, so the district court’s judgment of invalidity was *reversed* here as well.
4. Myriad’s claims to methods of analyzing BRCA gene sequences and comparing those with cancer-predisposing mutations to normal or wild-type gene sequences were held not to be directed to patentable subject matter. The district court’s decision was thus *affirmed* with respect to these claims.

Counting up the votes. Judge Lourie wrote the so-called “opinion of the court” that announces the judgment and gives the rationale. Judge Moore wrote a concurring opinion, meaning that she joined all aspects of the judgment. She also agreed with Judge Lourie’s reasoning with respect to the method claims and the patentability of isolated *cDNA* sequences. However, she had a slightly different reason for upholding the patentability of *DNA* sequences, and decided to explain her thinking at some length (31 pages!). Finally, Judge Bryson joined in the judgment with respect to the method claims and the patentability of longer sequences of *cDNA*. However, he voted against the patentability of all isolated *DNA* sequences as well as very short *cDNA* sequences, and would thus have affirmed the district court on that specific point. His somewhat more succinct opinion (19 pages) explains his thinking. Since he was in the minority on this point, his opinion does not have the force of law.

So, for those keeping score at home, here is how the judges came down on each issue:

1. *Standing*: 3-0, since one plaintiff has standing to challenge Myriad’s patents, the case can proceed.
2. *cDNA*: 3-0, *cDNA* is patentable (although for smaller *cDNA* molecules, the vote was 2-1, with Bryson dissenting).
3. *Method claims*: 3-0, with therapeutic screening claims upheld and comparing or analyzing claims invalidated.
4. *Isolated DNA*: 2-1, isolated *DNA* is patentable.

The majority’s rationale. With the bookkeeping out of the way, let’s take a look at how the judges reasoned their way through *Myriad*.

The plaintiffs’ standing. After opening with a genetics tutorial, the Lourie opinion addressed the very technical but nonetheless critical issue of *standing*. [As we discussed after the Myriad oral argument](#), standing is a constitutional question, and it boils down to whether the plaintiffs have a sufficiently direct and immediate interest in the outcome to be proper parties to file the case. Had the court found no plaintiffs to satisfy the threshold standing requirement, it would have dismissed the case without ever reaching the patent issues. The court found that there was standing, but it was very close.

Only one plaintiff—Dr. Harry Ostrer of (for the moment; more on that below) NYU Langone Medical Center—was held to have standing. That was because he alleged that Myriad forced him to stop offering BRCA clinical testing more than ten years ago by threatening infringement litigation, and that he remained ready, willing, and able to resume testing if the patents were held invalid. One plaintiff with standing was enough for the court to proceed to the merits.

It should be noted, however, that last Wednesday, just before the Federal Circuit released its opinion, [counsel for Myriad submitted a letter to the court](#) (pdf) alleging that Dr. Ostrer’s impending move from NYU to Albert Einstein College of Medicine deprives Dr. Ostrer, and thus the *Myriad* plaintiffs, of standing. While the Federal Circuit apparently did not see enough in Myriad’s last-minute letter to alter its standing analysis, the letter points out, correctly, that the standing requirement is an ongoing one which must continue to be met at all points during the appellate process. As *Myriad* heads through subsequent appeals (discussed below), the issue of the plaintiffs’ standing to maintain their challenge will continue to loom in the background.

Turning to the product claims (the so-called “gene patents”), Judge Lourie reviewed more than 100 years of cases dealing with all kinds of substances with natural precursors or analogs. He identified—correctly, in our view—the two key authorities as the Supreme Court’s opinions in [Chakrabarty](#) (holding genetically engineered bacteria to be patentable subject matter) and [Funk Brothers](#) (holding unpatentable an inoculum that combined bacterial species not known to co-exist in nature). He concluded that the test was whether the claimed substances were “markedly different—have a distinctive chemical identity and nature”—from the naturally-occurring version.

The patentability of DNA. cDNA sequences presented the easiest question for the court. Even Judge Bryson agreed that cDNA is generally patentable, since it is a human-made molecule and the body does not naturally contain DNA in exactly this form (with introns spliced out). However, as discussed below, Judge Bryson would have ruled differently with respect to particularly short sequences (as few as 15 base pairs) of cDNA.

When it came to the product claims, the real controversy concerned isolated genes and sequences in DNA form. The district court had focused on the similarity in function and information content between natural and isolated genes, downplaying the chemical and structural differences that patent lawyers and the USPTO had always relied on. [As Judge Sweet wrote last year](#) (pdf):

DNA represents the physical embodiment of biological information, distinct in its essential characteristics from any other chemical found in nature. It is concluded that DNA’s existence in an ‘isolated’ form alters neither this fundamental quality as it exists in the body nor the information it encodes.

Sixteen months later, Judge Lourie came down on the other side, focusing on the “cleaving” of isolated DNA out of its chromosomal environment as conclusive evidence of its fundamentally different nature. (Curiously, he claimed that “cleaving” DNA from its chemical environment is fundamentally different from “isolating” a substance from an impure environment, which has sometimes been held insufficient to support patentability.)

The arguments about whether isolated DNA is sufficiently distinct from its natural counterpart are well-known, and neither side has an absolutely compelling case. It seems to come down to an economic value judgment, and the Lourie and Moore opinions both reflect this reality. Both majority judges put great emphasis on the dangers of upsetting thirty years (and 2,654 isolated DNA patents, by Judge Lourie’s count) of what Judge Moore called “settled expectations and extensive property rights.” Both counseled deference to Congress, while Judge Lourie was “particularly wary” about a lower court expanding on an exception to patentability (the product of nature doctrine) that comes out of Supreme Court case law, not the Patent Act itself.

The method claims. The judgments from the court on both categories of method claims were unanimous, as noted above. Recall from our previous articles that the state of the law (such as it is) on methods generally is reflected in [the Supreme Court’s confused and confusing 2010 decision in *Bilski v. Kappos*](#). That case focuses on whether a method patent claims abstract processes (unpatentable) or specific applications (patentable), and expresses particular concern about method patents that preempt all uses of an abstract process. In addition, *Bilski* held that the Federal Circuit’s machine-or-transformation (MoT) test could not be used exclusively, but could be an “important clue” to patentability.

In *Bilski*, the Supreme Court declined to provide any guidance for the proper application of the MoT test in a biotechnology context. However, [earlier this summer the Supreme Court agreed to review the Federal Circuit’s decision in *Prometheus v. Mayo*](#), which has twice upheld the patentability of a method of administering a drug, determining the level of the drug in a patient’s bloodstream, and then adjusting the dosage accordingly to maximize therapeutic efficacy.

Myriad’s analysis and comparison claims failed the test completely, earning a solid “F” from the Federal Circuit. Judge Lourie wrote that such claims lack any “necessarily transformative step” and, in the end, “recite nothing more than the abstract mental steps necessary to compare two different nucleotide sequences.”

Myriad’s claim on a method of screening potential cancer therapeutics, on the other hand, was “not so manifestly abstract as to claim only a scientific principle.” It also passed the still-breathing MoT test, since it involves the “transformative” steps of growing host cells in the presence or absence of a cancer therapeutic and then determining and comparing their growth rates.” This was viewed as fundamentally different from simply comparing two DNA sequences.

Returning to the unpatentable claims to the analysis and comparison of DNA sequences, it is striking how much Judge Lourie emphasized the semantics of patent claim-drafting. With *Prometheus* undoubtedly on their minds, Myriad’s lawyers had argued that this method actually did involve transformation. They pointed out, for example, that here, just as in *Prometheus*, there was a “determining” step—in this case, of “the sequence of *BRCA* genes by, e.g., isolating the genes from a blood sample and sequencing them.” Judge Lourie noted, though, that this step, while described elsewhere in the patent, was not part of the *claims*, by which patentable subject matter must be exclusively judged. In *Prometheus*, by contrast, the determining step was in the claims.

It is hard to read this as anything but an invitation to patent lawyers to bring methods as abstract as Myriad’s within the ambit of patentable subject matter simply by putting more (perfunctory?) technical detail in the claims themselves. [As we have written previously](#), if clever draftsmanship is all that is ultimately required to satisfy the MoT test in many instance, the courts will have created “a potentially enormous opening through which to push all manner of personalized medicine patents replete with diagnostic, measurement, correlation and other interpretive or mental steps.”

The isolated DNA dissent. Judge Bryson argued in the same terms as the majority about the isolated DNA claims, and then reached the opposite conclusion. Taking on Judge Lourie’s cleaving argument, he wrote that “there is no magic to a chemical bond that requires us to recognize a new product when a chemical bond is altered or broken.” Agreeing with the district court about the paramount importance of the information content of genes, he concluded that “what is claimed in the *BRCA* genes is the genetic coding material, and that material is the

same, structurally and functionally, in both the native gene and the isolated form of the gene.”

Perhaps more significantly, Judge Bryson also reached the opposite conclusion with respect to the economic implications of invalidating Myriad’s patents. The—to him—“breathtakingly broad” claims to cDNA and DNA sequences as short as 15 nucleotides led Judge Bryson to look beyond the possibility of overturning biotechnology’s “settled expectations” and to the future effect of “a thicket of patents.” This patent thicket, at least to Judge Bryson, presents “a significant obstacle to the next generation of innovation in genetic medicine—multiplex tests and whole-genome sequencing.” He made a further point that we can confirm on the basis of our own experience: that “the costs involved in determining the scope of all those patents [in the thicket] could be prohibitive.”

Judge Bryson also departed from his colleagues in declining to give any deference to the USPTO’s 30-year practice of allowing isolated gene patents, on the grounds that it had never done any serious analysis of the subject matter issue. Judge Bryson’s argument was buttressed by the [Department of Justice’s amicus brief last fall, which advocated a dramatic departure from the PTO’s prior gene patent practice](#), as well as by a citation to an article by one of us (John) detailing the PTO’s limited review of these issues.

What happens next in *Myriad*? Since both Myriad and the plaintiffs both won and lost, both parties are eligible to seek further review, and both probably will. One possibility is to ask the Federal Circuit for *en banc* review by all of its active judges (currently ten) sitting together. This is relatively rarely granted, but more often in the Federal Circuit than in other federal courts of appeals because of its judges’ penchant for split decisions and major disagreements about fundamental doctrine. So it is a real possibility.

After review *en banc*, or sooner if that appeal is not granted, both parties could petition for *certiorari* (cert), or further review, by the Supreme Court. The Court grants cert in fewer than 100 cases in most years, denying the vast majority of cert petitions. However, the Court has taken more patent cases in recent years, and this is an important one, with obvious economic and scientific implications, so it is a promising candidate.

But—remember that the Court already has *Prometheus* on its docket, which could settle the methods questions present in *Myriad*. Among the possibilities here (yes, that was a reference to [Monty Python’s Spanish Inquisition skit](#)) are: (1) the Court takes the whole *Myriad* case; (2) it takes only the product claims issues, assuming that the method issues will be settled—at least for future cases—by *Prometheus*; (3) it takes *Myriad* and consolidates it wholly or in part with *Prometheus*, which would likely delay both cases until the 2012 term; or (4) it denies cert in *Myriad* and lets the Federal Circuit’s ruling stand as is. All we can know for sure is that *Myriad*, still, likely has quite a ways to go before a final resolution.

What does the *Myriad* decision mean for the real world? First and foremost, this opinion restores—at least for the time being—the gene *product* patent world to the state it was in before the district court’s bolt out of the blue last spring. So one reaction is, move along, people, nothing to see here. But we emphasize *at least for the time being*.

As we said, this case has miles to go before it sleeps. And it was a 2-1 decision, so the anti-gene patent position is neither crazy nor hopeless. Judge Lourie ended up making a very debatable call (on how different isolated genes are from their natural counterparts) on which reasonable minds can differ. Judge Moore was sufficiently dissatisfied with Judge Lourie’s reasoning that she took 31 pages to explain her own, ultimately (in our view) adding very little.

So there remains a high probability that there will be more said about the patentability of (in particular) isolated DNA sequences, probably by the courts (either the Federal Circuit *en banc*) or the Supreme Court, and possibly by Congress (if they ever manage to fix their debt ceiling distractions).

That said, how much difference will the final product patent decision in this case really make? Myriad’s own product patents will begin to expire in 2014. By the time *Myriad* wends its way through all available appeals, the biotechnology industry and clinical geneticists may have, collectively, innovated their way around the patents held by companies like Myriad.

Recall Judge Bryson’s fears about the impact on whole-gene sequencing. Are those fears justified? Judge Lourie repeatedly stressed *cleaving* the claimed isolated gene out of its natural environment. Whatever you think of that argument in the context of the isolation of single genes, [do present and forthcoming whole-genome sequencing technologies require the same cleavage](#)? In other words, do/will those technologies infringe patents on isolated DNA sequences using the analysis presented in *Myriad*? That question has yet to be fully and formally asked, and will almost assuredly not be addressed by the *Myriad* litigation. Which means that, whatever the outcome in this case, patent litigators with Ph.D.s in genetics should remain gainfully employed for the foreseeable future.

We should also look beyond the threshold question of patentability under Section 101. As we have written previously, [the real action on gene product patents is occurring under other sections of the Patent Act](#) that deal with novelty, non-obviousness, and the written description requirement. These sections’ requirements have been repeatedly tightened, with an overall effect of “[nibbling around the edges](#)” of gene patents, as we have put it. The *Myriad* court’s reference to all of these sections—none of which is in play here—underscores the point that passing the subject matter test barely gets you out of the batter’s box, let alone to first base.

We have also written (e.g., [here](#)) that the disposition of method claims, in *Myriad* but also in *Prometheus* and other cases, will ultimately prove more important to the personalized medicine industry. This case—unanimously—invalidates some of the broadest diagnostic method claims. But even that rejection comes across as relatively toothless, given that Judge Lourie offered a roadmap for the alert patent lawyer to reword such claims so that they might survive. That’s good news for those who might profit from broad method claims, cause for concern for those who might be inhibited by them, and a clear reminder that plenty more work (and, likely, litigation) is yet to come.

Ultimately, as *Myriad* pushes into its third year, our advice remains the same as before: keep watching—not just *Myriad*, but *Prometheus* as well, which is running slightly ahead on a parallel track—and know that, while the debt ceiling may yet cave in around us, whether the pigs will

ultimately rule the gene patent sky remains to be seen.