

Federal Circuit Issues Long-Awaited Opinion on Patenting of Genes



BY WILLIAM (BILL) GAEDE

May a gene be patented? Or does a gene belong to all of humanity? It has long been held in the United States that inventions reflecting the “hand of man” can be patented. It also has been long established that products of nature, abstract principles, or natural phenomena may not be patented, but the applications of abstract principles or natural phenomena may. Since the early 1980s, the United States Patent and Trademark Office (PTO) has issued patents on isolated DNA sequences, but the issue of whether such patents were patentable subject matter had never been challenged in court. On July 29, the U.S. Court of Appeals for the Federal Circuit held that isolated DNA sequences were patentable subject matter, but affirmed a lower court’s ruling that methods of comparing gene sequences did not constitute patentable subject matter.

Background

In May 2009, various individuals, medical researchers, and organizations represented by the American Civil Liberties Union (ACLU) filed suit in New York challenging gene patents held by Myriad Genetics (Myriad). The patents cover two genes—BRCA1 and BRCA2—and methods for correlating mutations in

Bill Gaede is a partner with McDermott, Will & Emery LLP in Menlo Park, Calif.

those gene sequences. Mutations in the genes are detected through a Myriad-developed diagnostic test used to determine whether a woman is predisposed to breast and ovarian cancers. According to plaintiffs, Myriad has threatened to sue any entity that provides the diagnostic test or entities that perform research on BRCA1 and BRCA2 mutations.

The ACLU suit sought effectively to overturn a long-standing policy of the PTO that isolated gene sequences are patentable subject matter. Congress on several occasions in the past has considered, but not passed, legislation addressing whether there should be restrictions on the ability to patent genes.

On March 29, 2010, Judge Robert W. Sweet of the U.S. District Court for the Southern District of New York answered the question by granting the plaintiffs’ motion for summary judgment in *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, 09-CV-4515. The highly significant ruling found that Myriad’s patent claims directed to isolated DNA sequences, methods of detecting BRCA mutations, and methods of using cells transformed with BRCA to screen for potential drugs are unpatentable subject matter under 35 U.S.C. § 101.

Specifically, for the claims directed to just isolated DNA encoding the BRCA1 or BRCA2 proteins (or fragments thereof), Sweet held these claims were unpatentable subject matter because they claimed a product of nature. In doing so, Sweet held that products isolated from nature must possess “markedly different characteristics” from the product in nature to constitute patentable subject matter. Further, Sweet said, DNA is “distinct in its essential characteristics from any other chemical found in nature [and its] existence in an ‘isolated’ form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes.”

Myriad’s method patents claimed methods of detecting BRCA mutations in a patient. Sweet held these claims invalid because the claimed methods constituted unpatentable abstract mental processes of comparing or analyzing two gene sequences, and the claimed steps of analyzing and comparing failed to recite the specific transformative steps that are a hallmark of patentable subject matter. Sweet further noted that even if the analyzing or comparing steps were interpreted to include

the steps of isolating DNA from a patient and sequencing that DNA, these transformative steps would be nothing more than data-gathering, which is insufficient to meet the transformation requirement.

Myriad's cell-screening patent claimed methods of identifying compounds useful in treating BRCA-associated cancer by screening compounds against cells transformed with BRCA. Again, Sweet held these method claims failed the transformation test because the transformative steps were mere data-gathering. In a footnote, Sweet rejected the argument that drugs that affect the BRCA cell impart a patentable transformation for the claim because compounds that fail in the screen would have no such transformative effect.

The Federal Circuit's Decision

Myriad appealed this broad ruling and on July 29, the U.S. Court of Appeals for the Federal Circuit reversed in part and affirmed in part Sweet's ruling. Writing for the majority, Judge Alan D. Lourie said, "We reverse the district court's decision that Myriad's composition claims to 'isolated' DNA molecules cover patent-ineligible products of nature under [Section] 101 since the molecules as claimed do not exist in nature." Based on a "markedly different characteristics" standard articulated in the Supreme Court's *Diamond v. Chakabarty* decision, Lourie wrote that isolated DNA has "markedly different chemical characteristics" compared to corresponding native DNA.¹

As to the patentability of isolated DNA sequences, the court found that the Supreme Court "has drawn a line between compositions that, even if combined or altered in a manner not found in nature, have similar characteristics as in nature, and compositions that human intervention has given 'markedly different' or 'distinctive characteristics.'" Applying this test, the court found that human intervention gave the specific isolated DNA sequence "markedly different characteristics" than the DNA sequence as it existed in nature:

In this case, the claimed isolated DNA molecules do not exist in nature within a physical mixture to be purified. They have to be chemically cleaved from their chemical combination with other genetic materials. In other words, in nature, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity. In fact, some forms of isolated DNA require no purification at all, because DNA can be chemically synthesized directly as isolated molecules.

Lourie did not accept the lower court's finding that because the information content of the sequence was similar to that found in nature, an isolated DNA sequence could not constitute patentable subject matter. He rejected such "a categorical rule," writing that it ignored "the distinctive nature" of isolated DNA molecules, which have "markedly different chemical structure." In doing so, he further rejected the government's "magic microscope test," which proposed that if an imaginary microscope "could focus in on the claimed DNA molecule as it exists in the human body, the claim covers unpatentable subject matter."

¹ The Federal Circuit decision also addressed the issue of whether there was a case or controversy. The court found that there was, and thus addressed the merits discussed above.

On the method claims, the court wrote that "Myriad's method claims directed to 'comparing' or 'analyzing' DNA sequences are patent ineligible; such claims include no transformative steps and cover only patent-ineligible abstract, mental steps." The court recognized under the Supreme Court's *Bilski v. Kappos* decision that assessing whether a claim includes transformation still remains an important and useful clue to patentability of method claims. The court ultimately struck down the Myriad correlation claims, finding no transformative step in the claims themselves. As the court said, "[T]he claims are instead directed to the abstract mental process of comparing two nucleotide sequences."

In doing so, the court rejected that merely limiting the correlation to "a particular technological environment" would render the claims patentable. The court further went on to reject Myriad's argument that a transformation occurred in the claims because the claims required inherently extracting DNA from a human sample and sequencing that DNA. As the court said:

The claims do not specify any action prior to the step of "comparing" or "analyzing" two sequences; the claims just recite the one step of "comparing" or "analyzing." Moreover, those terms' plain meaning does not include Myriad's proposed sample-processing steps; neither comparing nor analyzing means or implies "extracting" or "sequencing" DNA or otherwise "processing" a human sample.

Finally, the court found that the Myriad method claim directed to screening compounds with cells transformed with mutant BRCA were patent eligible. The court found the necessary "transformation" in the claim's steps of "growing a transformed eukaryotic host cell" and "determining the rate of growth of said host cell."

Judge Kimberly A. Moore filed a concurring opinion, distinguishing between sequence claims directed to isolated cDNA or short isolated sequences, and isolated sequences that are identical to naturally occurring sequences, which would present a "much closer call." Judge William C. Bryson dissented in part as to shorter or longer sequences that were isolated from nature, stating that such sequences would not constitute patentable subject matter. He would find cDNA claims to be patent eligible.

Next Steps and Ramifications

It is expected that the ACLU/plaintiffs will consider requesting a rehearing en banc at the Federal Circuit and/or petition for certiorari at the Supreme Court. The Supreme Court may very well accept certiorari, as it recently accepted certiorari in *Prometheus Laboratories Inc. v. Mayo Collaborative Services*. That case examined whether method claims directed to optimizing the dosing of specific drugs used to treat gastrointestinal autoimmune diseases were patent-eligible. The Federal Circuit characterized the issue as "whether Prometheus's asserted claims are drawn to a natural phenomenon, the patenting of which would entirely preempt its use . . . or . . . only to a particular application of that phenomenon," which would be patent eligible.

While the ACLU suit has garnered substantial publicity, for the life sciences industry, what are some of the

practical ramifications? At the outset, even if patent-eligible, traditional isolated DNA sequence claims, such as are present in the Myriad patents, are more difficult to patent today than in the past. This is because of the prior art that has developed over the last 30 years around gene sequencing and methods for isolating gene sequences. Federal Circuit decisions illustrating this trend are *In re Kubin*, where an unknown gene is obvious in view of an antibody to the product of the gene, and *In re Gleave*, where a full-length prior art gene anticipated antisense oligonucleotides. The life science industry has largely moved past relying on such isolated DNA sequence claims as a cornerstone of its patent strategies, given this body of prior art that did not exist when the patent office first began issuing isolated DNA patents.

As to the method claims that were invalidated, they arguably pose an issue for personalized medicine and diagnostic patent claims that rely on identifying and correlating gene mutations to disease states or treatments. But Lourie pointed the way to patent claim limitations that arguably would have preserved the patentability of the Myriad sequence comparison claims. As discussed above, had there been express limitations of

sequencing a patient sample or “processing” a human sample, the outcome may well have been different. Further, Lourie contrasted the claims in the Myriad case to those in *Prometheus*. He wrote that the *Prometheus* claims expressly contained a limitation of “determining” the drug’s metabolites levels in the subject, which necessarily required the transformative step of some form of extraction of the metabolites from the bodily sample. He then wrote:

Myriad’s claims, in contrast, do not include the step of “determining” the sequence of BRCA genes by, e.g., isolating the genes from a blood sample and sequencing them, or any other necessarily transformative step.

By implication, had the Myriad claims contained such broad express limitations, they may very well have constituted patentable subject matter.

Finally, the Supreme Court may accept the case for hearing and ultimately differ with the Federal Circuit. In other words, for the life sciences industry, the last word likely has not been rendered on whether isolated DNA sequence claims and methods for comparing gene mutations constitute patentable subject matter.