Containing *Myriad*

August 21, 2013 Michael Shuster and Kevin Kabler

Fenwick
FENWICK & WEST LLP

On June 14, 2013, a unanimous Supreme Court decision in *Ass'n for Mol. Pathology v. Myriad Genetics, Inc.*, held that Myriad's claims directed to "...a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated." 569 U.S. ___ (2013), Slip Op. at 18. In addition, the Court held that "...cDNA is patent eligible because it is not naturally occurring." *Id.*

What remains unclear is the reach of the *Myriad* holding to other patented inventions that also rely on "isolation" as the basis for patent eligibility. A number of useful and commercially-valuable therapeutics are isolated forms of naturally-occurring products such as proteins (e.g., fully-human monoclonal antibodies). Following *Myriad*, the validity of claims directed to such isolated products may soon be called into question in U.S. courts or by examiners at the U.S. patent office.

Containing the reach of *Myriad* in such venues will ultimately require patent practitioners to explain why *Myriad* should be limited to DNA and not extended to other naturally-occurring products (that were not at issue in *Myriad*). Without offering more, success may be difficult to come by since the parallels between isolated DNA molecules encoding naturally-occurring (i.e., genomic) sequences and isolated therapeutic proteins originally expressed within cells harboring these genomic sequences are so readily apparent. Isolating these molecules from their natural source allowed them to be characterized and exploited in new and previously unimaginable ways. The novel utilities of such isolated therapeutic molecules have provided the theoretical underpinnings for their patent eligibility. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911). Now, after *Myriad*, mere isolation may not suffice to confer patent eligibility, raising the spectre that therapeutic proteins encoded by any organism's genome also may be excluded from patent eligibility as a "product of nature."

It can therefore be challenging to see a path for continued patent eligibility of other biologically-encoded molecules if *Myriad's* holding is construed to mean that DNA molecules carrying genomic sequences are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material. However, in explaining its decision, the *Myriad* Court pointed out that: "genes *and the information they encode* are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material." Slip Op. at 18 (emphasis added).

The Court's language suggests that two overlapping but distinct considerations were fundamental to its holding regarding the patent ineligibility of isolated DNA:

1. Identity of the isolated DNA sequence and the corresponding naturally-occurring DNA sequence; and
2. The informational content utility of a naturally-occurring DNA sequence, i.e., the inherent, passive code provided by an ordered sequence of A, G, C, and T.

In *Myriad*, the Court continuously laid the groundwork for the inseparable nature of DNA sequence and the information it encodes by referring not just to DNA as a sequence, but instead as an information-containing sequence: "Sequences of DNA nucleotides contain the information necessary to create strings of amino acids, which in turn are used in the body to build proteins." Slip Op. at 2. "DNA's informational sequences and the processes that create mRNA, amino acids, and proteins occur naturally within cells." Slip Op. at 3. "It

is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes." Slip Op. at 11-12.

In its ensuing legal analysis, the Court made clear that it was not analyzing the claimed subject matter merely for the claimed DNA sequence alone, stating: "Nor are Myriad's claims saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a nonnaturally occurring molecule. Myriad's claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA." Slip Op. at 14. Instead the Court focused its analysis primarily on the informational content of the DNA sequence, stating that the claims "…understandably focus on the *genetic information* encoded in the BRCA1 and BRCA2 genes …[and are] …concerned primarily with the *information contained in the genetic sequence*, not with the specific chemical composition of a particular molecule." Slip Op. at 14-15 (emphasis added).

Finally, the Court clarified its holding, stating: "We merely hold that *genes and the information they encode* are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material." Slip Op. at 18 (emphasis added).

This analysis suggests that two fundamental elements are *both* needed to find ineligibility for an isolated compound under §101: identity of structure *and* informational content. The statement that "…genes *and* the information they encode are not patent eligible…" indicates that the Court considered both elements, suggesting that the absence of a single element may be enough to avoid ineligibility of an isolated compound. *Id*. This reading, that two elements may both need to be present to find ineligibility, is strengthened by the Court's holding regarding cDNA, which contains the same information as naturally occurring DNA but is structurally distinct from naturally occurring DNA.

Given the claims at issue in *Myriad* itself, cDNA presents the primary test case with an ascertainable outcome available for consideration of the necessity of each element. In *Myriad*, the Court defines cDNA as DNA containing "…the same protein-coding information found in a segment of natural DNA…" Slip Op. at 1. However, in addressing the patent eligibility of cDNA the Court does not consider this informational content enough to void its eligibility and instead holds that: "cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a 'product of nature' and is patent eligible under §101…" Slip Op. at 17. Thus, the Court defined cDNA as meeting only one element (informational content) but still considered it patent eligible due to sequence-based differences with naturally occurring DNA (structural identity).

The Court also discussed another factual situation in *Myriad* that falls outside the scope of the holding: "Nor do we consider the patentability of DNA in which the order of the naturally occurring nucleotides has been altered. Scientific alteration of the genetic code presents a different inquiry, and we express no opinion about the application of §101 to such endeavors." Slip Op. at 18. Situations involving nucleotide substitutions that create a nucleotide sequence distinct from its naturally occurring parent sequence, but that still encode an identical protein, present one of the more challenging inquiries in this regard. However, if each element were applied as it was to cDNA it is likely that such substituted nucleotide sequences would be considered patent eligible since they are structurally distinct from the naturally-occurring sequence even though they both encode the same protein. Given the Court's holding that simple removal of non-coding introns from a naturally occurring sequence is enough to confer patent eligibility for cDNA, this seems likely to be the correct outcome following *Myriad*. Instead, obviousness likely presents the more relevant legal consideration for such situations.

Therapeutic proteins present a situation similar to that presented by cDNA. While cDNA is structurally distinct from naturally-occurring DNA (cDNA lacks intron sequences), it is unlikely that many isolated therapeutic proteins bear significant structural

differences to their naturally occurring counterparts. Even if minor physical differences could be ascertained in an isolated therapeutic protein, it is unlikely that a court would consider such differences to be "enough" given the holding of *Myriad* and the fact that minor differences that exist between isolated and genomic DNA were well documented for the Court. *Association of Molecular Pathology* v. *United States Patent and Trademark Office*, 689 F. 3d 1303, 1328 (CA Fed. 2012). However, therapeutic proteins are different from cDNA in that they do not inherently contain information in the same way that DNA does, i.e., the amino acid sequence of a protein does not passively convey any downstream information in and of itself. Their sequence is not a "code" for anything in the way that DNA codes for mRNA or that mRNA codes for a protein. Instead their sequence of amino acids represents building blocks that combine to form a whole with a function distinct from passive information conveyance. Thus, applying each element to an isolated therapeutic protein suggests that patent eligibility should still exist for such compounds under §101, i.e., isolated therapeutic proteins are similar to cDNA in that they only meet one element (structural identity) but could reasonably be considered patent eligible since their sequence does not inherently convey information in the unique way that DNA does (informational content).

This analysis and outcome is further supported by policy considerations that likely influenced the Court and caused it to highlight the informational content of DNA so heavily throughout the *Myriad* opinion. Myriad's claims to naturally-occurring DNA were enforced in a way that prevented individuals from freely accessing their own genetic information without paying a toll to Myriad first; however claims to isolated, naturally-occurring proteins do not present such a concern. The basic utility of an isolated therapeutic protein is different from that of isolated DNA because therapeutic proteins are primarily useful for performing functions such as binding to other proteins whereas, in the diagnostic arena, DNA is solely useful for its informational content. In other words, public policy and the utility considerations of §101 may have influenced the Court's holding regarding patentable subject matter more than was explicitly stated in the *Myriad* opinion. This fundamental difference in utility between DNA and therapeutic proteins underlies the second element used to find patent ineligibility for DNA: The informational content of a DNA sequence, i.e., the inherent, passive code provided by an ordered sequence of A, G, C, and T.

At present it is unclear whether the courts will expand or restrict the reach of *Myriad* beyond DNA. However, patent practitioners can work toward restricting *Myriad's* ultimate reach by providing more than a conclusory statement that *Myriad* should be limited solely to DNA. Advocating for consideration of each element (structural identity and informational content) in the context of isolated products such as therapeutic proteins can provide a cogent argument that can be combined with others to increase the likelihood of limiting *Myriad*'s reach to DNA alone.

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