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U.S. Supreme Court Holds Human Gene Patent Claims Are Invalid

PORZIO UPDATE

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On June 13, 2013, the United States Supreme Court published its decision in *Ass'n For Molecular Pathology et al. v. Myriad Genetics, Inc*., Slip Op. No. 12-398 (S.Ct. June 13, 2013), which reversed the U.S. Court of Appeals for the Federal Circuit's decision with respect to the patentability of isolated DNA gene sequences. The Supreme Court held that the patent claims at issue extended to DNA in its natural form and, thus, were not subject to protection under the U.S. patent laws. The high Court stated that although Myriad found an important and useful gene, "Myriad did not create anything" and that "separating that gene from its surrounding genetic material is not an act of invention."

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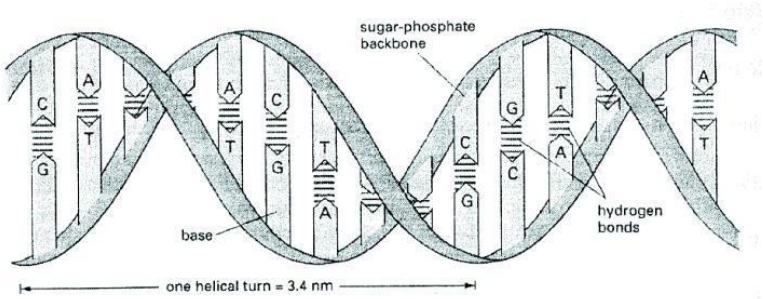
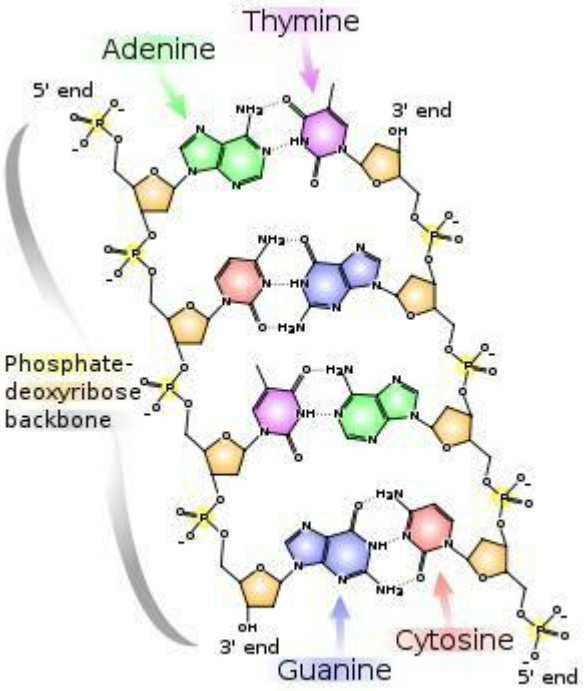
Genomic DNA

The term DNA is an acronym for the chemical compound, deoxyribonucleic acid. In its natural state, DNA exists as a double helix comprising two strands of a sugar phosphate backbone joined together by repeating units of four nucleotide bases -- adenine (A), thymine (T), cytosine (C), and guanine (G). In a DNA molecule, one part of each base is covalently bound to the one strand of backbone, and another part of a base binds to a corresponding base bound to the opposite strand, i.e., A binds to T, and C binds to G, to form a "ladder" structure, which is twisted into a helical form. The linear order of the bases in a DNA molecule is referred to as its sequence.

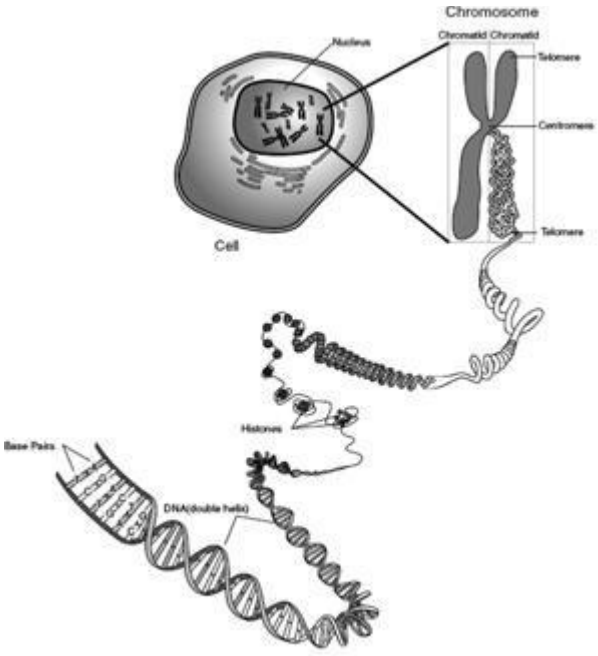
Thus, a very simplified version of the DNA double helix is depicted as follows:



A more detailed chemical structure of DNA looks something like this:



"Native" or "genomic" DNA exists in almost every human cell. Genomic DNA is packaged into 23 pairs of chromosomes. On the chromosomes, DNA exists as complex structures comprising extensively folded, extended DNA molecules wrapped around proteins such as histones:



The 23 pairs of chromosomes make up the human genome.

Isolated DNA

Isolated DNA is not found in nature, and is not wrapped in histones. It is a modified and smaller, free-standing portion of larger, natural DNA. Isolated DNA has been cleaved, i.e., its covalent bonds in the backbone have been chemically severed, and the molecule excised from the genome has been chemically altered.

The work of scientists in the fields of molecular biology, biochemistry, and organic chemistry includes the discovery, isolation and synthesis of DNA and genes. Genes are segments of the genome that are associated with the production of proteins that consist of the structures and constituents of the body, which regulate chemical reactions in the body, or, in the case of genetic mutations, are associated with disease states or other anomalies.

In simple terms, certain molecules in a cell, such as RNA molecules, aid in the transcription and translation of DNA into a protein or other polypeptide. A group of three bases, e.g., ATG, acts as a code, i.e., a "codon," that is transcribed by messenger RNA (mRNA), and translated by cellular machinery, such as a ribosome, which uses that codon to produce an amino acid. Sequences of codons, i.e., genes, cause the ribosome to manufacture strings of amino acids. Proteins and other polypeptides are comprised of amino acids linked together. A large part of what DNA does is to provide the "genetic code" by which proteins are manufactured by our cells.

The biotechnology industry includes the manufacturing of proteins in laboratory settings by, very simply stated, using isolated genes that are incorporated into viruses or other vectors, such as plasmids, and then inserted into cells, which are then harvested and grown. The cells use their machinery to produce the proteins that the inserted genes code for. As the number of cells grows, so does the amount of protein. This process, which was developed in the late 1970s, was used to manufacture virtually unlimited amounts of proteins such as human growth

hormone and insulin, which proteins had been previously obtained by the laborious and expensive extraction from the organs of dead animals. (The author was involved in patent litigation concerning these inventions). Today, large numbers of useful proteins are inexpensively produced in large quantities using these biochemical methods, resulting in dramatic increases in available medicines, amongst other things. Isolated genes are also useful as diagnostic tools, and as probes used in helping to identify genetic mutations, as well as in cloning techniques. As a result, biotech enterprises, and research universities and institutions, have evolved into a huge worldwide industry that contributes immensely to public health and knowledge, generates billions of dollars, and employs many thousands of people.

Isolated gene patents are some of the bedrocks of the biotech industry. The isolated genes and the processes described in the previous paragraph have been the subject of several thousands of patents for over three decades. As to an isolated gene, the typical patent claim covers a particular isolated gene sequence that codes for a protein. It has been the law, and the understanding of the biotech industry, that such patent claims are valid, and that these patents do not extend to genomic or native DNA. The limited right to exclude provided by the patent laws helped fund and nurture many well-known biotech companies. However, many scientists, academics and members of the public believe that the biotech industry was patenting human life, i.e., genes as they exist in nature, and that pharmaceutical and biotech companies are blocking research and hindering the practice of medicine. So came the *Myriad* case.

The Myriad Case and the BRCA Gene Patents

Years ago, Myriad discovered that certain mutations in the human genome, known as BRCA 1 and BRCA 2, were linked to increased risk of breast and ovarian cancer. It identified the genetic basis of their link to cancer risks using an analysis called positional cloning. Subsequently, using chemical techniques, they isolated and excised these genes from the human genome, and were awarded patents that claimed, *inter alia*, isolated DNA sequences coding for the desired proteins and polypeptides. A typical Myriad patent claim at issue in the case covered: "[a]n isolated DNA coding for a BRCA 1 polypeptide," which has "the amino acid sequence set forth in SEQ ID NO:2."

In 2009, a case to invalidate Myriad's gene patents was brought in the United States District Court for the Southern District of New York by The Association for Molecular Pathology, certain university scientists, patient advocacy groups, individual patients, the American Civil Liberties Union (ACLU), and others who claimed an interest in striking down gene patents. The plaintiffs won the case, and Myriad appealed to the Federal Circuit, which reversed and ruled that isolated DNA does not exist in nature and can be patented, and issued other related rulings. The plaintiffs appealed to the Supreme Court, which remanded the case back to the Federal Circuit. On remand, the Federal Circuit reaffirmed its prior holdings. On September 25, 2012, the ACLU and others petitioned the Supreme Court to take the case on the merits, which it did. On June 13, 2013, the Supreme Court issued its ruling.

The Core Issue Of Patent Eligibility For Gene Patents

The key question before the courts in the *Myriad* litigation was whether the patents at issue covered products of nature or chemical compositions made by human hands.

The governing law in this area, particularly as set forth and summarized in the Supreme Court's decision in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) held that genetically engineered bacteria, useful in treating oil spills, was patentable because the claimed micro-organism did

not exist in nature. Rather, its was "made by the hand of man." The Supreme Court in *Myriad*, and the Federal Circuit, agreed that *Chakrabarty* was the guide post for their conflicting decisions. In a nutshell, *Chakrabarty* and its precedents and progeny stand for two general rules:

> (1) the subject matter that is eligible for patenting is very broad, virtually "anything under the sun made by the hands of man/[woman],"
> (2) however, not everything can be patented - laws of nature, abstract ideas, and products of nature cannot be patented.

Thus the *Myriad* case boiled down to one key question: were Myriad's isolated gene claims directed to (a) chemical compositions made by human handiwork, or (b) products of nature?

The Federal Circuit held that they were directed to the former:

> It is undisputed that Myriad's claimed isolated DNAs exist in a distinctive chemical form--as distinctive chemical molecules--from DNAs in the human body, *i.e.*, native DNA. Natural DNA exists in the body as one of forty-six large, contiguous DNA molecules. Each of those DNA molecules is condensed and intertwined with various proteins, including histones, to form a complex tertiary structure known as chromatin that makes up a larger structural complex, a chromosome. . . . Inside living cells, the chromosomes are further encapsulated within a series of membranes and suspended in a complex intracellular milieu.
>
> Isolated DNA, in contrast, is a free-standing portion of a larger, natural DNA molecule. Isolated DNA has been cleaved (*i.e.*, had covalent bonds in its backbone chemically severed) or synthesized to consist of just a fraction of a naturally occurring DNA molecule. For example, the *BRCA1* gene in its native state resides on chromosome 17, a DNA molecule of around eighty million nucleotides. Similarly, *BRCA2* in its native state is located on chromosome 13, a DNA of approximately 114 million nucleotides. In contrast, isolated *BRCA1* and *BRCA2*, with introns, each consists of just 80,000 or so nucleotides. And without introns, *BRCA2* shrinks to approximately 10,200 nucleotides and *BRCA1* to just around 5,500 nucleotides. . . . Accordingly, *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.

The Supreme Court disagreed, mainly on the basis that, even if the patent claims covered "isolated" genes, isolation of the genes did not change the fact that the locations and coding sequences of the patented genes were the same as the locations and coding sequences of their corresponding genomic or native genes. Importantly, a high point in the language of the Supreme Court's ruling is directed to the manner in which the patent attorneys chose to draft the claims:

> 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. Instead, the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA 2 genes. If the patents depended upon the creation of a unique molecule, then a would-be infringer could arguably avoid at least Myriad's patent claims on entire genes . . . by isolating a DNA sequence that included both the BRCA1 or BRCA2 gene and one additional nucleotide pair. Such a molecule would not be chemically identical to the molecule "invented" by Myriad.

However, Myriad's patents also had claims directed to isolated complementary DNA (cDNA), and the Supreme Court upheld the validity of these claims. cDNA is a form of DNA artificially synthesized from a messenger RNA template. It was undisputed that the patent claims to isolated cDNA, which differed from the natural gene sequence because they had their introns removed (an intron is a segment of a gene that does not function in coding for protein synthesis), were patentable because the claimed cDNA sequences only contained the coding nucleotides, and, thus, they could be used to express a protein in a cell which does not normally produce it.

Conclusion

The Supreme Court's decision to invalidate Myriad's patent claims has potentially far-reaching consequences for the future of the biotech and pharmaceutical industries that depend upon isolated gene patents for a variety of economic and scientific reasons. (However, the Supreme Court left intact Myriad's patent claims for cDNA because those were directed to synthetic molecules, not products of nature.) The decision also presents future challenges to the patent bar with respect to the assessment of patentability, as well as patent claim drafting, and raises a number of social and legal issues as to the scope and impact of the U.S. patent laws, especially insofar as the biosciences venture further into the development of inventions that touch on the use of genetic and chemical materials to change the course of human life.

The author welcomes your inquiries and comments.