Personalized medicine patent law update

Issues surrounding patenting of nucleic acids and other biotech inventions

This is an article for anyone who is interested in learning more about Personalized Medicine and the legal issues surrounding it, written by someone with a deep background as both a scientist and a lawyer. The article focuses on Personalized Medicine patent law issues. Recently, many nucleic acid-based inventions have been deemed unpatentable subject matter.
Here new case law and USPTO Guidelines will be described, as well as strategies for patent protection of biotech inventions.

BACKGROUND

A patent gives the patent owner the right to exclude others from making, using, selling, or importing the invention. It is difficult to patent a biotech product because such inventions are increasingly said to lack subject matter eligibility by Courts and the USPTO. However, there are strategies that can increase the likelihood of successfully obtaining a biotech patent.

Keyw[1]ds

Nucleic acid, patent, subject matter eligibility, 35 U.S.C. §101, personalized medicine

SIGNIFICANCE OF A PATENT

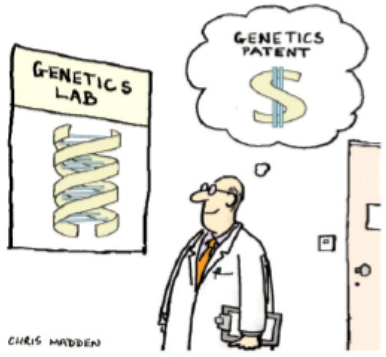
What is the value of a patent? Currently, two biotech companies are contesting ownership of CRISPR gene-editing patents. These patents allegedly are worth $1 billion and supposedly have attracted similar venture capital. Thus, these types of patents can be highly valuable.

PATENTING PROCESS

So now we understand that biotech patents can be highly valuable, how do we get one? The patenting process begins with filing an invention disclosure at the USPTO, which is evaluated by an Examiner according to rules called the US Code. These rules require that the invention must involve patentable subject matter (35 USC 101); must be novel (35 USC 102); must be non-obvious (35 USC 103); and must be sufficiently described (35 USC 112). The first requirement, subject matter eligibility, has been in controversy regarding nucleic acids.

SUBJECT MATTER ELIGIBILITY

Recently, the Supreme Court heard a case involving the company, Myriad Genetics, for patents directed



to a DNA-based, breast cancer test. Myriad was sued by its competitors who said that the patents were invalid. The Court held that claims pertaining to isolated DNA sequences identical to those found in nature are NOT patent eligible subject matter. In the past however, isolated DNA sequences have been patentable.

PERSONALIZED MEDICINE DEFINED

The Myriad case focused on personalized medicine, where a person's DNA is sampled, then analyzed, to determine whether the person carries a genetic marker for a certain disease. A treatment plan is developed based on drugs known to be most effective to limit that disease. For example, the drug/antibody, Herceptin ®, is effective in patients who express high levels of the DNA sequence for HER-2. Another example is the drug, Gleevec ®, which is prescribed for patients having chronic myeloid leukemias. Personalized medicine can be extremely successful in prolonging life because it involves a targeted treatment rather than a trial and error approach. It is the future of medicine and DNA is the crux of it.

Myriad's patents were for diagnostic tests based on the sequence of two genes, BRCA1 and BRCA2. It was known that certain mutations of these genes increase the chance of breast and ovarian cancer, from a normal rate of 12% to 85% for breast and 50% for ovarian . Some people who are found to have the mutations choose to have preventive surgery to remove the tissue, while others take specific drugs known to inhibit cancer growth. There is an increased chance of survival if these cancers are caught early.

Myriad patents claimed an isolated fragment of genomic DNA having the BRCA1 or 2 sequence, which were found to be patent ineligible. Other claims were directed to a short fragment of cDNA containing only the exons of the BRCA1 gene. These were also found to be patent ineligible since they read on the natural DNA sequence. However, a longer fragment of cDNA that did not read on the natural sequence was found to be patent eligible.

SUBJECT MATTER ELIGIBILITY

The Supreme Court stated that separating that gene from its surrounding genetic material is NOT an act of invention. The Court explained that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes or the known cancer mutations. Thus, the isolated genomic DNA sequences that are identical to those found in nature were not patent eligible.

However, if you read between the lines of the Supreme Court decision, an isolated DNA sequence including one additional nucleotide pair would NOT be chemically identical to the naturally occurring gene. Likewise, the longer DNA that contained the exons only, the cDNA, was different than that found in nature and was patentable. Thus, DNA that is chemically different from natural DNA can be patentable.

35 USC 101

35 USC 101 states that any new and useful process, machine, manufacture, or composition of matter is patentable. However, laws of nature, natural phenomena, and abstract ideas are not patentable. In the biotech arts, laws of nature refer to screening tests and diagnostic methods, for example. Natural phenomena refer to natural products such as nucleic acids, peptide fragments, vaccines, and host cells, for example. How "different" does a nature-based product have to be in order to be patentable?

SUBJECT MATTER ELIGIBILITY TEST

Here's the test. Ask whether the claim is directed to a process, machine, or composition of matter. If the answer is yes, then ask whether the claim is directed to a law of nature, a natural phenomenon, or an abstract idea. These are judicially recognized exceptions to patentability. If that answer is no, then the claim is patentable. If that answer is yes, then ask if the claim recites additional elements that amount to significantly more than the judicial exception. If not, then the claim is not patentable.

Most important in light of recent case law is that invention must be a new composition of matter. Unfortunately, that is not how Myriad's claims to the BRCA sequences were expressed. Myriad didn't claim the nucleic acids as a new chemical composition nor did they focus on the chemical changes that resulted from the isolation of a particular section of DNA. Instead, their claims focused on the genetic information encoded in the BRCA1 and BRCA2 genes, namely the DNA sequence.

USPTO GUIDELINES

The USPTO provided a set of Guidelines on how to claim biotech inventions that suggest that nature-based products must show markedly different characteristics than the natural product itself. Here are some examples.

- Claim 1: An isolated DNA comprising SEQ ID NO: 1.

The natural gene is described by SEQ ID NO 1 and the claimed isolated DNA has the same sequence. The isolated DNA has different structural characteristics than naturally occurring gene because the chemical bonds at each end of the DNA strands were severed in order to isolate it from the chromosome on which it occurs in nature. This is true but, under the holding of Myriad, this isolated but otherwise unchanged DNA is not patent eligible because it is not different enough from what exists in nature. The claimed DNA has no different functional characteristics either, because it encodes the same protein as the natural gene. Thus, the claim does not qualify as patent eligible subject matter.

- Claim 2: An isolated DNA comprising a sequence with 90% identity to SEQ ID NO: 1.

The claim is limited to DNA containing a non-natural modification relative to the natural gene sequence. The DNA structure is different and the function may be different than the natural gene. This claim has patent eligible subject matter.

- Claim 3: The isolated DNA of claim 1, further comprising a fluorescent label.

The claim includes DNA with a fluorescent label, which does not occur in nature. This difference rises to the level of a marked difference, and so the claimed molecule qualifies as patent eligible subject matter.

STRATEGIES FOR PATENT PROTECTION

While isolated DNA may not be patentable at the moment, methods of using it may be. Be sure to include method claims in addition to the composition claims in patent applications. Include the DNA sequence in the method claims, which provides some protection. Avoid reciting purely mental steps, such as comparing a nucleic acid sequence to a reference nucleic acid sequence. This may be found to be an abstract idea, which is not patentable.

Some other suggestions are to include a "transformative" step where the actual physical step is recited, such as extracting, sequencing, or detecting. Also, include the use of a machine. Add a step regarding the adjustment of the dosage or treatment after analysis. Lastly, try to include details such as specific materials and reagents.

COMPOSITION CLAIMS

For composition claims, recite a combination of genes or biomarkers instead of just one. Highlight the structural and functional differences between the inventive molecule and the naturally occurring DNA. Describe the DNA as a chemical compound, not merely by its sequence. Recite the cDNA sequence. Include a heterologous nucleotide in the natural sequence. Delete a nucleotide from the sequence at one or more points. Substitute a base analog, sugar analog, non-natural linkage or backbone derivative into the natural sequence. Add a non-native excipient such as an adjuvant, a salt, or a vehicle for storage or delivery. Recite the nucleic acid sequence as part of an expression construct. Incorporate a regulatory sequence in an unnatural position. Fuse the nucleic acid with a heterologous sequence. Recite the dosage form. Add a detectable tag, marker or label. Bind the nucleic acid to a substrate or other molecule. Recite a different function or utility. Include the DNA as part of a kit. Thus, there are many ways to successfully obtain patent claims based on nucleic acids.

PATENT PROSECUTION STRATEGY

During patent prosecution, include specific and broad claims in patent applications. Highlight the chemical nature of nucleic acid derivatives in the specification and conversations with Examiners. Emphasize the significance of the invention to patient health. Include an expert declaration describing the unconventional nature of the nucleic acid. Lastly, because isolated DNA applications are still patentable in Europe and Asia, file patent applications on this subject matter abroad.

SUMMARY

Personalized Medicine will be increasingly used in the future for the diagnosis and treatment of disease. It is important to understand the current laws regarding patentability of biotech inventions and how to gain patent protection for your valuable intellectual property.

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