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Will the patentability of genes survive?

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Recent court decisions in the United States and Europe have brought the patentability of genes under attack.

Introduction

After an approximately 30-year reign during which patents were issued for genes, the issuance of such patents has come under scrutiny in both the United States and Europe. On March 29, 2010, in *Association for Molecular Pathology v. United States Patent and Trademark Office*, a US district court invalidated 15 patent claims to genes used to diagnosis susceptibility to breast cancer and likely responsiveness to certain therapeutics^{1, 2, 3}. In Europe, an administrative review panel within the European Patent Office invalidated claims to these same genes in a counterpart European patent⁴. In the United Kingdom, the court invalidated a patent for an identified gene on the grounds of lack of industrial applicability⁵.

The question becomes whether gene patents will survive when the issue reaches higher courts. This article discusses the reasoning by the US and European courts for invalidating the patent claims to genes and concludes with a look at the economics and politics at play, as well as one possible solution— compulsory licensing.

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Reversing conventional wisdom

For approximately three decades, the reasoning that a purified gene isolated from the remainder of the contents of a living cell from which it came, in a quantity or concentration greater than that in the living cell, was a human intervention that substantially altered that which was naturally occurring so as to have new character and use, was considered sound. For example, a gene as it was found in a cell could not be used in an assay. To be used in an assay, the gene had to be isolated and increased in quantity and concentration. Accordingly, the isolated and concentrated gene had a different character and use than the naturally occurring gene. The genes that were the subject of *Association for Molecular Pathology*, held by Myriad Genetics, were located using correlation studies between cancer and DNA markers, which were in turn used to map the location of the gene within the genome. The process of identification and sequence analysis took over two years and cost over \$100 million. In his decision, Judge Robert Sweet revisited this conventional wisdom and concluded that DNA's existence in an 'isolated' form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes. Therefore, the patents at issue directed to 'isolated DNA', containing sequences found in nature are unsustainable as a matter of law and are deemed unpatentable subject matter under 35 U.S.C. §101⁶.

Judge Sweet reasoned that US Supreme Court precedent mandated that for an article of manufacture and/or composition of matter to be a patentable subject, it had to be "markedly different" from a product of nature. He also concluded that there is no patentable subject matter absent a change that results in the creation of a "fundamentally new product." Judge Sweet picked up the "markedly different" standard from the Supreme Court case of *Diamond v. Chakrabarty*⁷. In *Chakrabarty*, the invention in question was bacteria that "ate up" oil in an oil spill. The Court wrote that: "the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own..."⁸.

However, in what sense did the Supreme Court use the term "markedly different characteristics"? Did the Court use this phrase in the sense of establishing a standard, or in the sense of judicial hyperbole to praise the invention and bolster its decision of patentability? In its *Manual of Patent Examining Procedure*, the US Patent and Trademark Office analyzed the *Chakrabarty* decision and did not extract that the Court imposed a "markedly different characteristics" standard⁹. Further, there is also a question of whether the phrase "fundamentally new product" appears in Supreme Court precedent. Even more so, by applying a

question of whether the phrase “fundamentally new product” appears in Supreme Court precedent. Even more so, by applying a “markedly different” standard, Judge Sweet relieved himself of fully reasoning out the patentability of gene fragments, which in fragmented form do not appear naturally in a cell, involve a measure of ingenuity to deduce the operative region of the gene and have properties that increase the efficacy of molecular diagnostics.

Judge Sweet redressed the *a priori* reasoning that isolation of a gene was a human intervention that substantially altered the naturally occurring gene to impart new character and use by honing in on a passage from *The American Wood-Paper Co. v. The Fibre Disintegrating Co.*, where the high court stated, “There are many things well known and valuable in medicine or in the arts which may be extracted from divers[e] substances. But the extract is the same, no matter from what it has been taken. A process to obtain it from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture”¹⁰.

Judge Sweet rejected as nonanalogous the Fourth Circuit case of *Merck & Co., Inc. v. Olin Mathieson Chem. Corp.* In *Mathieson*, the Court found a claim for vitamin B₁₂ produced by artificial fermentation in a concentration greater than 450 LLD units per milligram to be patentable over naturally occurring vitamin B₁₂, which is found in cow liver and rumen in “minute quantities.” The court distinguished the highly concentrated vitamin B₁₂ from a purified substance as being different in kind from that found in nature. In particular, the court wrote that, “From the natural fermentates, which, for this purpose, were wholly useless and were not known to contain the desired activity in even the slightest degree, products of great therapeutic and commercial worth have been developed. The new products are not the same as the old, but new and useful compositions entitled to the protection of the patent”¹¹.

The patent owner in *Association for Molecular Pathology* argued that *Mathieson* was on point because native DNA was unsuitable to be a primer or probe in molecular diagnostic tests. Judge Sweet rejected this on the grounds that the isolated DNA possessed the identical nucleotide sequence as the natural DNA sequence and that the isolated DNA functioned as a primer or probe primarily due to the nucleotide sequence identity between native and isolated DNA¹².

A question arises whether Judge Sweet properly concluded that *Mathieson* was inapposite. A gene in a living cell is present in such low abundance that it cannot be used as found in the cell or purified out of cells in any quantity to be useful for an assay. Only through Myriad's technology of isolating the gene (or fragments) did a meaningful assay arise for breast cancer susceptibility and responsiveness to certain therapeutics. Further, once the human intervention in the isolation imparts the quality of being useful in an assay, is it or is it not superfluous that there is no additional human intervention to change the chemical form and structure? In *Mathieson*, the concentrated vitamin B₁₂ retained the same chemical form as natural vitamin B₁₂ so as to be physiologically active.

Judge Sweet found it unnecessary to address an argument that because DNA represents the physical embodiment of biological information, on this basis it is a phenomenon of nature and exempted from being patentable subject matter. Heretofore, patentability of chemical compositions has been premised on their physical structure. This argument to exempt a chemical composition on the grounds that it conveys information ventures into uncharted legal waters.

The patents that were the subject of the lawsuit contained method claims for a molecular diagnostic. Judge Sweet held these claims to be unpatentable by applying a “machine-or-transformation” test newly articulated by the US Court of Appeals for the Federal Circuit in *Bilski v. Kappos*¹³. This test was articulated by the Federal Circuit in the context of business method patents. Applying this test, Judge Sweet found the diagnostic methods to be unpatentable mental steps. At the time Judge Sweet made his ruling, *Bilski* was under review by the US Supreme Court. The Court has since issued its decision (*Nat. Biotechnol.* **28**, 767 (2010).) In brief, the Court recognized the machine-or-transformation test as being only one calculus to assess patentable subject matter and held that there could be other tests. This at least provides a basis for making creative argument in support of the patentability of the diagnostic claims found to be unpatentable abstract mental steps.

Challenges in Europe

In Europe, Article 5 of the European Patent Convention currently provides that:

1. The human body...and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

In a counterpart European patent originally issued covering both the genes and diagnostic methods, several oppositions were filed against the Myriad patent^{15, 16}. Ultimately, a second instance panel of review of the European Patent Office (EPO) sustained the validity of a narrower version of the patent claiming diagnostics but not claiming genes or gene fragments.

In the United Kingdom, the England and Wales High Court of Justice (EWHC) put the brakes on investigators running to the patent office as soon as a gene is identified and/or postulated without sufficient experimental data as to its function and implication regarding a disease state. In more detail, investigators using bioinformatics, and not wet chemistry, identified and/or postulated a particular human protein called neutrokine- α and deduced the nucleotide sequence of a gene that coded for this protein. A European patent was successfully obtained from and defended in the EPO claiming this gene¹⁷. The patent did not contain a description of a real and practical way to exploit the gene. In a revocation action, the EWHC declined to follow the EPO and invalidated the patent for want of industrial applicability in that its only known use was in research to learn how the gene itself might be implicated in a disease state¹⁸.

Conclusions

Economics seems to have been a contributing factor in the district court's decision. With Myriad Genetics charging \$2,000 to \$3,000 for its molecular diagnostic test resulting in a financial barrier for women receiving potentially lifesaving medical care, emotions ran deep and the political pressures were great for a result-oriented decision to make the diagnostic available at a more affordable price. Other diagnostic laboratories have claimed to be able to provide a similar test at a much lower cost, but were precluded from doing so by Myriad's patents. Hard cases make bad law¹⁹.

Rather than developing bad law, perhaps one solution lies in compulsory licensing of some patents. With copyrighted material, Congress has mandated compulsory licensing under certain circumstances²⁰. The Supreme Court has opened the door to compulsory licensing in its decision in *eBay Inc. v. MercExchange, L.L.C.* that a permanent injunction in a case of patent infringement is not automatic²¹. Germany and other countries have compulsory licensing. Compulsory licensing seems to be the vehicle for fairness and for everyone to get a slice of the pie. Innovative companies will be able receive a return on their investment in research and development and be encouraged to do so. Consumers will have access to the technology at reasonable prices and lives will be saved and good health achieved. It is up to disinterested parties to add the weight to make compulsory licensing a reality.

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