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The Myriad case: Genes are no invention!

On March 29, Myriad Genetics Inc (Myriad) lost a 'land mark' case over its US intellectual property comprising seven US patents. These patents gave Myriad exclusive control over various aspects of the human genes linked to breast and ovarian cancers: BRCA 1 and BRCA 2. The decision, handed down by Judge Sweet, a federal court judge of the US District Court for the Southern District of New York, is the first in US legal history dealing with the patentability of naturally occurring biological materials that have been 'isolated' from their natural environments. His decision has shaken the biotechnology industry around the world by reminding us all that patents are for 'inventions' not 'products of nature'.

BRCA 1 and BRCA 2 are genes located on human chromosomes 17 and 13, respectively. BRCA 1 was mapped in 1990 by Professor Mary-Claire King after 16 years of research, and was isolated within four years of Professor King's announcement. BRCA 2 was isolated the following year.

Every human being has these genes. However, the particular significance of these genes is that people, who carry mutations in the BRCA 1 and/or BRCA 2 genes, have a significantly increased risk of developing breast and ovarian cancers.

The genetic gold rush was in full swing in the early 1990s when Myriad was incorporated by Dr Mark Skolnick, a genetic researcher at the University of Utah, and Mr Peter Meldrum, his venture capitalist partner. The objective was to claim the patent prize which, as Dr Skolnick said recently, came in "isolating and discovering the underlying [BRCA] gene".

On the basis of the evidence before him, Judge Sweet concluded that isolated BRCA gene mutations and the proteins coded for by those genes were unchanged by their isolation from the human body.

The 'isolated' BRCA 1 gene became the subject of a US patent application, which then translated into US Patent 5,747,282 and Australian Patent 686,004 (under the Patent Cooperation Treaty). The 'invention', other than being 'isolated', was identical to the naturally occurring BRCA 1 gene. To isolate the gene Skolnick's team had simply removed it from the human body. This US patent application, however, laid the ground work for a series of US and other patents granted around the world over the BRCA 1 gene and its use in diagnostics and other medical technologies. The same occurred with BRCA 2, except that in Europe Myriad was pipped at the post by the UK's Cancer Research Campaign Technology Limited (CRCTL) which filed a European patent application a few weeks before Myriad filed its US patent application giving it priority over Myriad's. While this threw a spanner into the works, Myriad continued to successfully secure patents all over the world over BRCA 1 and BRCA 2 genes and their use in diagnostic testing.

The angry reaction in Europe was palpable. Twenty-six organisations such as the Belgian Society of Human Genetics, Institute Curie and the British Society of Human Genetics joined forces to oppose Myriad's European patents granted by the European Patent Office. That fight only ended at the end of 2008 when the Technical Appeal Board of the European Patent Office reinstated Myriad's European patent over BRCA 1, albeit with modified claims. Even so, European clinicians, such as Dr Dominique Stoppa-Lyonnet from the Curie Institute, maintain that the modified claims are unenforceable. According to her, "the patent ruling won't stop us testing the gene in France".

And while this very public brawl tempered Myriad's ability to exclusively control BRCA gene testing in Europe, there was, seemingly, little opposition in the United States and Myriad was able to exert complete and exclusive control over all BRCA genetic testing. As a result, a full BRCA genetic test currently costs US$3,200 and is undertaken by Myriad's laboratory in Utah.

But the strength of Myriad's monopoly in the US has been severely weakened by Judge Sweet's decision. Consistent with "the clear line of Supreme Court precedent and accompanying lower court authorities, stretching from American Wood-Paper through to Chakrabarty" Judge Sweet held that the "purification [or isolation] of a product of nature, without more, cannot transform it into patentable subject matter".

In the US Supreme Court's famous 1980 decision in Diamond v Chakrabarty, Chief Justice Berger (who wrote the majority 5:4 decision) made it clear that although US patent law was flexible enough to permit the patentability of a genetically modified bacterium created using the techniques first invented by Stanley Cohen and Herbert Boyer in 1973, the bacterium had to display "characteristics markedly different to anything found in nature" before a product of nature could no longer be defined as "nature's handiwork". What persuaded the US Supreme Court in Chakrabarty to hold that the GM bacterium in question satisfied the test was its ability to degrade crude oil.

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This function was not something any naturally occurring bacterium could perform.

On the basis of the evidence before him, Judge Sweet concluded that isolated BRCA gene mutations and the proteins coded for by those genes were unchanged by their isolation from the human body. Applying Chakrabarty he held:

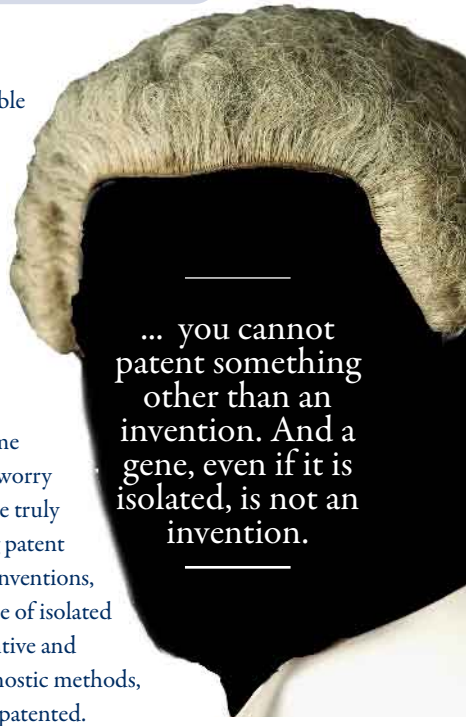
Because the claimed isolated DNA is not markedly different from native DNA as it exists in nature, it constitutes unpatentable subject matter under 35 USC § 101.

That, however, only loosened Myriad's stranglehold on BRCA testing slightly.

The decisive blow came when Judge Sweet held that the use of these biological materials in diagnostic tests was also not patentable subject matter for two reasons. First, the method claims were "nothing more than data-gathering steps to obtain the DNA sequence information on which to perform the claimed comparison or analysis". Second, "in the absence of a specified method for isolating and sequencing DNA" the method claims were "meaningless" and would "fail the 'machine and transformation' test under § 101".

Finally, he hammered the last nail in the BRCA patent coffin by invalidating the claims directed to "'comparing' the growth rates of cells in the presence or absence of a potential cancer therapeutic". In his opinion the method claims sought to monopolise "a basic scientific principle: that a slower rate of cell growth in the presence of a compound indicates that the compound may be a cancer therapeutic" and therefore they too failed for the reason that they "represent nothing more than preparatory, data-gathering steps to obtain growth rate information".

Myriad has announced that the decision will be appealed to the US Court of Appeals for the Federal Circuit (CAFC). And whatever the outcome it is reasonably foreseeable that the CAFC's decision will be appealed to the US Supreme Court. A final determination is many years away. However, Judge Sweet's decision now represents the law in the United States and will continue doing so until it is overturned (if it is ever overturned).



... you cannot patent something other than an invention. And a gene, even if it is isolated, is not an invention.

The decision has worried some commentators but it should not worry biotechnology companies that are truly innovative and which are seeking patent protection for biotechnological inventions, that is, inventions which make use of isolated biological materials in new, inventive and useful ways. New therapies, diagnostic methods, even cures, will still be able to be patented. This decision merely reinforces the basic premise of patent law that you cannot patent something other than an invention. And a gene, even if it is isolated, is not an invention.

Paul D. R. MacLeman
CHIEF EXECUTIVE OFFICER, GENETIC TECHNOLOGIES LIMITED (GTG)

Services and gene patenting: GTG

Genetic Technologies has always operated within the existing legal and patent framework.* Should the rules change, the company will operate within the new rules.

In order to offer the BRCA tests we secured the legally issued Australian Myriad patent – and pay a substantial fee for the right to offer these tests. Some government funded laboratories and research organizations illegally do not pay, are providing quasi commercial pathology services and enjoying larger profit margins.

Should this patent protection be removed in Australia, Genetic Technologies would benefit financially as it would no longer stand out as the entity in Australia paying royalties for tests such as BRCA.

Despite the American district court decision at the end of March, we anticipate a lengthy appeal process that will probably reach the American Supreme Court. This decision should in no way be regarded as final.

However the intellectual benefits of patent protection serve a greater good in the longer term.

While we are watching the BRCA genes case, the issue is much greater than this. Take the example of the HER2 gene. Discovery of this gene was the catalyst for development of the widely used breast cancer treatment Herceptin. Without patent protection this life prolonging drug may never have been developed.

Genetic Technologies is a small, efficient biotechnology company employing 80 highly qualified Australian scientists, customer service and business people. This company is regarded as Australia's foremost private genetics lab. Its priority is to provide the world's best gene testing and cancer testing for Australians.

Should this patent protection be removed in Australia, Genetic Technologies would benefit financially as it would no longer stand out as the entity in Australia paying royalties for tests such as BRCA.

By providing a private BRCA testing service, we are able to determine the risk profile for women in as little as two weeks. Before Genetic Technologies provided this test in Australia the public institutions providing this service typically took many months, sometimes years, to provide results to women vulnerable to breast cancer.

Patent protection massively contributes and is necessary for new drug development and better diagnostics. Why would effort and resources be devoted to discovery in Australia if the patent incentive were to be removed. Australia would be out of step with the rest of the world and its successful history of medical research would have a final chapter.

**Genetic Technologies was an early pioneer in recognising important new applications for 'non-coding' DNA. The Company has since been granted patents in 24 countries around the world, securing intellectual property rights for particular uses of non-coding DNA in genetic analysis and gene mapping across all genes in all multicellular species.*