FINANCIER WORLDWIDE corporatefinanceintelligence

REPRINTED FROM:
SEPTEMBER ISSUE 2011

Are genes patentable?

BY SIMON O'BRIEN AND DAVID GASS

Recombinant DNA technology sparked the biotechnology explosion that has exponentially expanded our understanding of biology and reshaped medicine in the past three decades. Amazingly, the fundamental question of patent-eligibility of recombinant DNA inventions is still being settled, on both sides of the Atlantic.

'Gene patents' in the US

Section 101 of the US patent law provides that, subject to meeting other patentability requirements, "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter ... may obtain a patent therefor...." The US Supreme Court has construed this provision broadly: while laws of nature, physical phenomena, and abstract ideas are not patentable, "anything under the sun that is made by man" is patentable. Under this guidance, the US Patent and Trademark Office (PTO) has, for decades, granted 'gene patents' directed to nucleic acids isolated by man from their natural environment.

This longstanding practice was called into question by a declaratory judgment challenge by several parties to the validity of selected claims in a portfolio of patents owned by or exclusively licensed to Myriad Genetics. The 'gene patent' claims at issue pertained to isolated DNA molecules comprising all or portions of gene sequences known as BRCA1 and BRCA2, useful in testing for genetic predisposition to cancers.

On 29 March 2010, on a motion for summary judgment, the US District Court for the Southern District of New York issued a 156 page decision in *Association for Molecular Pathology et al. v U.S. Patent & Trademark Office et al. ('Myriad')* declaring the patent claims at issue invalid, shocking the biotechnology industry. With potential implications for claims in hundreds or thousands of other US patents, the court decided that the claims to the isolated BRCA genes and gene fragments were invalid under Section 101 because the claims encompass "products of nature". The defendant-patentee Myriad appealed this decision to the Court of Appeals for the Federal Circuit, which hears all patent appeals.

In an unusual development, the US Department of Justice (DoJ) filed an amicus brief with the Federal Circuit, ostensibly representing the position of the executive branch of Federal government, which includes the PTO. The DoJ urged the Federal Circuit to *affirm* the District Court's holding of invalidity with respect to certain claims directed to isolated DNA, but urged reversal with respect to other claims directed to cDNA, because cDNA does not exist in nature.

On 29 July 2011, a three judge panel of the Federal Circuit issued a 105 page split decision reversing the holding of invalidity of the isolated DNA claims – the focus of this article – while sustaining a holding of invalidity as to certain diagnostic method claims.

Writing a 'majority' opinion of the Court, Judge Lourie reasoned that all of the claims to isolated nucleic acids fell within the accepted statutory class of "compositions of matter", and that such compositions of matter were not unpatentable "products of nature" as held by the District Court. Central to Judge Lourie's opinion was that the inventors had created new molecules that did not exist in nature: "BRCA1 and BRCA2 in their isolated state are not the same molecules as DNA as it exists in the body; human intervention in cleaving or synthesizing a portion of a native chromosomal DNA imparts on that isolated DNA a distinctive chemical identity from that possessed by native DNA."

In a concurring opinion, Judge Moore agreed with Judge Lourie's decision, but not entirely with his reasoning. "I analyze the isolated DNA claims ... to determine whether they have markedly different characteristics with the potential for significant utility, e.g., an "enlargement of the range of ... utility" as compared to nature." Under this test, Judge Moore concluded that claims directed to cDNA's and claims directed to probe-size BRCA-1 or -2 DNA fragments were patent-eligible, because both cDNA's and probes were chemically different from natural DNA and had significant recombinant DNA and diagnostic utilities that native BRCA-1 and -2 chromosomal DNA lacked. However, she felt that broader claims covering all or most of a full length human BRCA gene sequence, presented a "much closer case" because she was unable to identify (from the litigation record) a compelling "enlargement of the range of utility" for these longer DNA sequences. Ultimately, Judge Moore was moved by "settled expectations" of the industry and the "substantial historical background" of the case, including decades of Patent Office practice issuing "thousands of patents with claims to isolated DNA" without Congressional interference. "I leave it to Congress, who 'has the constitutional authority and the institutional ability to accommodate fully the varied permutations of competing interests,' … to decide whether it is necessary to change the scope of section 101 to exclude the kind of isolated DNA claims at issue here. '[U]ntil Congress takes such action, this [c]ourt must construe the language of § 101 as it is.'" On this basis, Judge Moore sided with Judge Lourie, and the holding of invalidity of the 'gene patents' was reversed.

Judge Bryson concurred with the majority on the patent eligibility of claims directed to cDNA, but dissented with respect to the isolated nucleic acid claims covering gene fragments or full length BRCA coding sequences. Judge Bryson felt that the case dealt with a pure question of statutory interpretation and no deference was owed to established PTO practice, policy, or guidelines.

Thus, the Federal Circuit in *Myriad* has reconfirmed the patent eli-

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gibility of isolated DNA, but only by a 2-1 split decision, with Judge Moore opining that some of the claims presented a "close call". Moreover, each opinion could signal different approaches should the Federal Circuit consider the continued patent eligibility of other biotechnology inventions in the future, such as purified or isolated proteins and antibodies that exist, in impure form, in nature. The plantiffs-appellees are widely expected to request reconsideration by the Federal Circuit *en banc,* and/or review by the US Supreme Court, which may have the final word in the debate.

'Gene patents' in Europe

In Europe, the EU Biotechnology Directive (98/44/EC) was brought into force in 1998. Article 3 of the directive specifically provides that, subject to meeting the other patentability requirements, biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature. Article 5 goes on to provide that 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. However, for genes to be patentable, in addition to the other patentability requirements of novelty, inventive step, etc., it is necessary that the industrial application of the gene is disclosed in the patent application. These provisions were brought into effect in the European Patent Convention (EPC) in Rules 27 and 29.

In T 0666/05 the Board of Appeal of the European Patent Office considered a corresponding Myriad patent which had been granted but then opposed by a number of parties. The patent contained, amongst others, a claim to: "A nucleic acid probe having 15 to 30 nucleotides of SEQ ID NO:1 [the cDNA of the mutated BRCA1 gene] and containing the mutation 185delAG –> ter39".

In its opposition, Greenpeace NV argued that that the sequence of such a probe occurred in nature and was therefore a discovery rather than an invention. The board ruled on the argument. It stated that the claim related to a nucleic acid probe comprising a partial DNA sequence of the human BRCA1 gene, and it was described in the patent as having been obtained by technical processes. The probe was therefore ruled as being an isolated element of the human body as defined in Rule 29 EPC and Article 5 of the EU Biotechnology Directive. The board did not see the patentability of such gene sequences isolated from their natural environment to be a contentious issue. Indeed it is notable that, perhaps seeing its argument as a weak one under EP law, Greenpeace NV did not make this point during oral argument.

Nevertheless concern has been expressed by the industry following a decision from the European Court of Justice (ECJ) in C428/08 which related to Monsanto's patent to DNA sequences encoding a class of enzyme variants which are resistant to a specific herbicide. Monsanto claimed that the importation into Holland of soya meal made from plants expressing the patented DNA sequence, and which contained traces of the DNA, infringed the patent in Holland.

In this decision the ECJ looked at Article 9 of the EU Biotechnology Directive and considered how it should be interpreted for the importation into the EU of a patented DNA sequence in a product where the DNA was no longer performing its function.

Article 9 of the Biotech Directive reads as follows: "The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product is incorporated and in which the genetic information is contained and performs its function."

In answer to the question, the ECJ ruled that there is no protection for a DNA sequence 'as such' and that a patent directed to a DNA sequence may only cover that sequence when performing the function for which it is patented.

In this case, Monsanto's patent does not, therefore, extend to soya meal containing the patented gene where the gene is no longer performing its herbicide function.

Thus, while it is possible to obtain patents for DNA sequences in Europe, the ECJ's decision potentially reduces the scope of protection given to DNA patents.

Conclusion

The US Federal Circuit's acknowledgement that the patenting of genes has become the basis for a valuable industry is to be welcomed. It is hoped that the European courts in future recognise this value and do not interpret a 'DNA's function' so narrowly that significant medical advances will be impaired. ■

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