

Patents and public health

European institutions are challenging Myriad Genetics's patent monopoly on the *brca1* gene

An increasing number of international research and governmental institutions are challenging several gene patents, arguing that the patent holders' absolute control of diagnostic methods is not in the public's best interests. Most notably, the Institut Curie, a cancer research centre in Paris, is leading the fight against Myriad Genetics, a US biotechnology company that plans to install a monopoly on all genetic work associated with the breast

apparently singular control over diagnosis and therapeutic applications. 'No company should own this genetic information. This monopoly is an abuse of power,' explained Gilbert Lenoir, head of the research department at the Institut Gustave-Roussy, during a press conference at the Institut Curie in September, concerning the patent opposition.

The potential market for diagnosis and therapeutics based on the genetic predis-

position to cancer is big; and so are Myriad's plans. The company refuses to give any licences and demands that all DNA samples are sent to its testing laboratories in Salt Lake City, UT. Nevertheless, seventeen laboratories in Europe are still performing diagnostic tests based on the *brca1* sequence, which puts them at risk of being sued for patent infringement, regardless of the detection method they use. 'Theoretically, we can be sued,' said Jacques Warcoïn, the opponents' legal consultant at the Cabinet Régimbeau. But many think that this is a risk worth taking in light of the effects that Myriad's monopoly on genetic testing would have on health care. In June 2001, the Oncological Genetics Unit at the Institut Curie, headed by Dominique Stoppa-Lyonnet, demonstrated that the direct sequencing technology used by Myriad Genetics and their approach of

them to improve on or develop new diagnostic methods. And the cost of the test poses another barrier to health care—the mutation searches performed by Myriad have a price tag of €2744, as opposed to an estimated cost of €914 for the test performed in French laboratories. Myriad's monopoly would thus dramatically increase the cost of screening the population and put additional pressure on many European countries' social and medical systems. Such a commercial approach to health care also goes against the holistic way in which European countries view public health, as it would separate biological research and clinical investigation from patient care. 'It is often very important to have a global approach and to take into consideration the tests and the patients' perception of the tests,' said Stoppa-Lyonnet.

Finally, the collection of DNA samples by Myriad would constitute the only sample bank in the world and thus give the company ultimate control over the raw material. Critics fear that Myriad would gain another monopoly concerning future research on other breast cancer predisposition genes and enable it to file even more patents as a result of such discoveries. 'Giving the war treasure of research—that has been put into our hands by patients—to an industrial group, so that it can patent it, is a unpleasant track to follow,' said Thomas Tursz, head of the Institut Gustave-Roussy.

Since the Institut Curie started the initiative to denounce this 'abuse of power', many other European institutions have

Critics of Myriad's wide-ranging patent rights maintain that it not only prohibits further research on diagnostics and therapies but also has a detrimental effect on public health

and ovarian cancer predisposition gene *brca1*. The critics of Myriad's wide-ranging patent rights maintain that the company's absolute control not only prohibits further research on the diagnosis of and therapies against breast cancer, but also has a detrimental effect on public health.

Since the European Commission adopted a directive allowing human genes to be patented in July 1998, many such patents have been granted and indeed challenged, including the battles over the insulin, relaxin and hematopoietin genes. In 2001, seven years after Myriad Genetics first identified the sequence of *brca1*, the European Patent Office (EPO) granted the company three patents covering all potential diagnostic and therapeutic applications based on the gene's sequence. Several European research centres and associations quickly contested the first two patents in an attempt to fight Myriad's monopoly. More recently, in August 2002, the Institut Curie, the Institut Gustave-Roussy, the Assistance-Publique-Hôpitaux de Paris together with almost all European genetics societies and many scientific institutions and governments turned up the heat and filed a joint opposition notice to the third patent. As this protects the isolated gene and the corresponding protein, and includes all imaginable future therapeutic uses, such as gene therapy and screening of drugs or transgenic animals, the opponents aim to block the company's

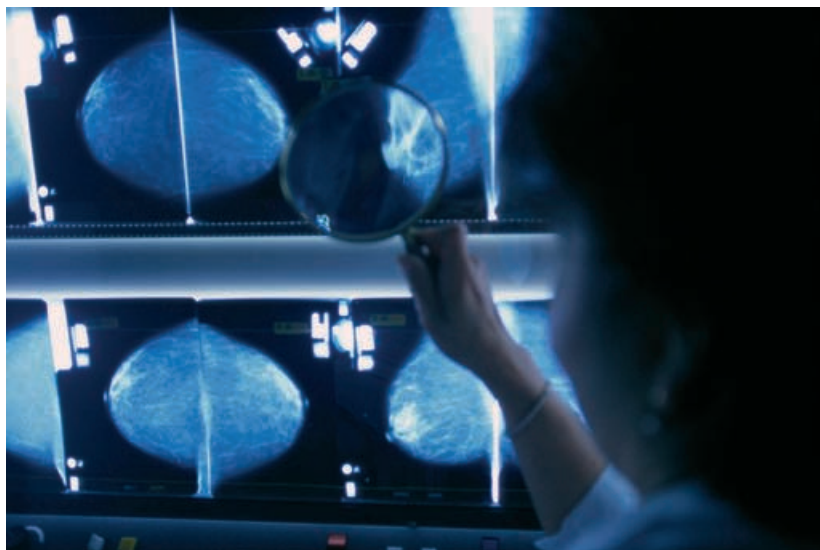
position to cancer is big; and so are Myriad's plans. The company refuses to give any licences and demands that all DNA samples are sent to its testing laboratories in Salt Lake City, UT. Nevertheless, seventeen laboratories in Europe are still performing diagnostic tests based on the *brca1* sequence, which puts them at risk of being sued for patent infringement, regardless of the detection method they use. 'Theoretically, we can be sued,' said Jacques Warcoïn, the opponents' legal consultant at the Cabinet Régimbeau. But many think that this is a risk worth taking in light of the effects that Myriad's monopoly on genetic testing would have on health care. In June 2001, the Oncological Genetics Unit at the Institut Curie, headed by Dominique Stoppa-Lyonnet, demonstrated that the direct sequencing technology used by Myriad Genetics and their approach of

Opponents might also opt for the *ex officio* licence, a French legislation that allows anyone to override drug patents if they are contrary to public health

only focusing on the detection of point or small-sized genetic abnormalities, failed to detect 10–20% of all expected mutations.

A further effect of the monopoly is that physicians and research scientists in Europe would lose their expertise in this field, as Myriad's patents do not allow

supported them. The Institut Gustave-Roussy, the Assistance-Publique-Hôpitaux de Paris, the Belgian human genetics society, the Belgian and Dutch human genetics centres and the German, Danish and British genetics societies, now all oppose Myriad's first patent. Concurrently, the European Parliament has passed a resolution



Physician examining mammographs.

supporting the French initiative and has invited 'other institutions of the European Union and the governments of the Member States to do likewise.' In February 2002, the Belgian Ministries of Health, Social Affairs and Scientific Research, the Dutch Ministry of Health and the German League against Cancer also declared their opposition to this patent. And after several European institutions filed a notice against the third patent in August, the Dutch and the Austrian Ministry of Health and the Swiss Social Democrat Party joined the movement.

To block these patents the opponents focus on three points. The first is a lack of priority and absence of novelty, because the gene sequence was already available in the scientific databases when the third patent was filed. The second argument is the lack of inventiveness for the same reason. The third point claims that the therapeutic uses, in particular gene therapy methods, were not sufficiently described for the purpose of implementing them effectively.

The EPO has already responded to the three opposition notices and is re-examining Myriad's patents, but it will take at least four years until the office eventually makes a decision. Opposition to a patent is a common occurrence—about 6% of all patents are challenged—and around two-thirds of these are successful, with the patent either revoked or muted to a limited form. Myriad, though, is not worried about the opposition. 'Myriad is confident in the validity of its issued patents,' said William A. Hockett from the

company's Corporate Communications department. 'In general, it is routine for patents with commercial potential to be opposed in Europe. Genentech's tissue plasminogen activator patent was opposed. Amgen's was opposed. Both of these patents were upheld and are major contributors to revenues,' he said. 'In the past, there have been cases with a lot of opponents and patents have been granted anyway,' Lenoir acknowledged.

Although nobody is able to predict the outcome of the challenge at this stage, the

European countries might be the forerunners in the debate about gene patents and ensuing monopolies

patent opponents are confident that they will prevail. A revocation of any of Myriad's patents on *brca1* would set a precedent for future challenges of monopolies on other genes patented by biotech companies. For instance, the US company Bio-Rad holds the hemochromatose gene (HFE) patent—another potentially huge market for diagnosis and therapies as genetic hemochromatose is the most common of all hereditary diseases—and is willing to apply the same industrial and commercial principles as Myriad Genetics. 'It is not only about breast cancer but about hundreds of gene patent applications. If nothing is done, it will be almost impossible to practice genetic analyses properly in the future,' said Gert Matthijs

from the Belgian Centres for Human Genetics.

In case the EPO does not revoke any of Myriad's patents, opponents might then opt for another solution called *ex officio* licence ('licence d'office'), a French legislation that allows anyone to override drug patents if they are contrary to public health. Roger-Gérard Schwartzberg, former French Minister for Research, and Bernard Kouchner, former French Minister for Health, both declared last year that they would support extending the French *ex officio* system to genetic diagnosis. If this provision were backed by other EU Member States, it would protect laboratories testing for *brca1* mutations, while not challenging Myriad's patent.

European countries may thus be forerunners in the increasingly important debate about gene patents and the ensuing monopolies. Indeed, other countries are already getting involved. Canada and Australia have both shown an interest in introducing legislative measures equivalent to the French *ex officio* system. In the USA, Representative Lynn Rivers of Michigan introduced a Bill in Congress in March 2002 to limit the claims of patent holders in the field of genetic diagnosis. The ultimate goal is to put the diagnostic tools at the disposal of the entire health-care system while enabling physicians and researchers to perform research in order to improve and perfect the testing techniques.

Nevertheless, this alternative would not resolve the recurring problem arising from how patents are currently issued. 'The specific nature of DNA as a carrier of genetic and private information requires special considerations, but actual patent law and the current interpretation by the EPO do not sufficiently reflect this special status,' said Matthijs. According to the EC directives that govern patentability, the mere discovery of an element of the human body, including the sequence or a partial sequence of a gene, cannot constitute a patentable invention. 'The human body can't be patented itself but when something is isolated from it, if there is something inventive about it, it can be patented. A function associated from a gene for a specific use is a good example,' said Siobhan Yeats, a biotechnology expert at the European Patent Office, explaining the office's interpretation of this directive. She defended the EPO in that its role is only to grant patents based

analysis

on criteria that do not include the prevention of monopolies on genetic diagnosis. 'The EPO is not responsible for what happens after we grant a patent,' Yeats said. 'The European Union and the European Parliament encourage filing patents for biotechnologies. We just conform to the law. We don't have an opinion on it,' she said. But she pointed out that the EPO has recently raised the requirements for such patents, which could be seen as a

sign of stricter control on gene patent deliveries.

A change in the law in favour of public health can only be achieved by the intervention of EU institutions, but the European Commission has not been forthcoming on this issue. 'The EPO will not react personally. The only institution that can have an influence on the EPO is the European Commission,' said Matthijs. 'We would like to discuss with the EPO to

make more modern interpretations of the European Patent Convention but they are not accessible this way. The European commission should organise forums where views could be exchanged on the issue of gene patents.'

Aude Lecrubier

DOI: 10.1093/embo-reports/kvf251