# A shot in the arm for gene therapy company

A patent covering all *ex vivo* gene therapy that was issued last month to the US National Institutes of Health (NIH) rocked both the academic world and the biotechnology industry.

Reactions ranged from criticisms that it was too broad or too obvious, to fears that it would hold back progress within the field of gene therapy. Others argued that issuing such a patent would help the biotechnology industry because it marked an important shift in policy at the US Patent Office.


**Michael Blaese and French Anderson, two of the three coinventors on the *ex vivo* gene therapy patent issued last month.**

The patent names as coinventors of *ex vivo* gene therapy French Anderson, Steven Rosenberg and Michael Blaese. They developed the technique while working at the NIH during the 1980s, and in 1990 treated four-year-old Ashanti De Silva who suffers from adenosine deaminase deficiency, a rare genetic blood disorder.

The work was cosponsored from the mid-80s by Gene Therapy Inc. (GTI) of Rockville, Maryland, under a Cooperative Research and Development Agreement with NIH. As a result of the cooperative agreement, the NIH was required to award an exclusive licence to GTI, and anyone wanting to work with the technique now needs to negotiate a sublicence with the company. There are exemptions, however, for most research and for companies gathering toxicology, safety and efficacy data to support applications submitted to the US Food and Drug Administration (FDA).

Those exemptions, according to Robert Abbott, president and chief executive officer of the biotechnology company Viagene of San Diego, California, might mean that a company would only mount a challenge if its research eventually produced a product for which it wanted FDA approval. It will be several years before anyone will be in a position to make such an application, thus a challenge to this patent may also be some way in the future.

Others point out that sublicensing is common practice for the biotechnology industry and that broad-based patents, such as that held by Stanford University for basic techniques in recombinant DNA technology, have not held back research. Anderson, who became chairman of GTI's science advisory board in 1991 when he left the NIH, says that it is not GTI's intention to hold up research. He points out that the US government, through the NIH, holds the patent, which should afford rival companies some guarantees that they will be able to sublicense the technology.

Given the breadth of the patent, rival companies certainly need that assurance. Its main claim covers the removal of cells from the body, the introduction of new genetic material, and reintroduction of the altered cells into the body where they can produce a protein that alleviates or cures an illness resulting from faulty genes. In other words it covers all *ex vivo* manipulation of all cell types with any vector that leads to the *in vivo* expression of therapeutic levels of a protein.

As is usual practice when filing for a patent, the NIH and GTI initially sought a much broader patent than they expected to receive. In this case: all of gene therapy, including both *ex vivo* and *in vivo* manipulations. As is usual practice, the patent office then whittled the claim down.

Even so, many still consider the patent too broad, and like Krishna Dronamraju, president of the Foundation for Genetic Research in Houston, Texas, they are sure that it will be challenged. In particular, speculation was rife that Somatix of Alameda, California, or Targeted Genetics of Seattle, Washington, would be the ones to mount such a challenge. Both companies are associated with scientists who have developed aspects of *ex vivo* gene therapy. However, the lawyer for Somatix and a spokeswoman for Targeted Genetics say they are still assessing the situation.

That assessment comprises a careful examination of something called the 'file wrapper', a dossier including all of the correspondence between an applicant and the patent office. Only this document, released on issuance of the patent, will show whether the patent is as broad as it seems and whether there are grounds for a challenge.

And even as such an examination is under way, the field of gene therapy is moving from *ex vivo* to *in vivo* genetic manipulations. Part of the rational being that once the science and technology are well enough understood, *in vivo* techniques will be simpler and cheaper.

That move is not immediately apparent from a look at a breakdown of the 100 protocols that have already been approved by NIH's Recombinant DNA Advisory Committee (80 per cent are for *ex vivo* gene therapy). In spite of these statistics, industry is for the most part moving toward *in vivo* techniques. And Anderson's laboratory at the University of Southern California in Los Angeles is now working only on *in vivo* gene therapy. Last month in the midst of the to-do about his *ex vivo* gene therapy patent, Anderson and three colleagues filed a patent application for *in vivo* gene therapy for breast cancer.

This move towards *in vivo* techniques is, however, slow. Only now are researchers moving from toxicology to efficacy trials for *ex vivo* techniques and it will be years before such therapies are routinely available.

In fact, it is because gene therapy has not yet provided proof of efficacy that many in the biotechnology industry were excited by this patent. For some time the biotechnology industry has been concerned that the patent office was behaving like the FDA and demanding too much proof of utility before awarding a patent. Representatives of the biotechnology industry believe that this situation has contributed to the scarcity of capital, because investors are concerned that without patents and the attendant licences and sublicences their investment would not be protected.

So, even if the patent is challenged, it has shown that the patent office is moving away from what has been a deeply unpopular position and has once again focused the spotlight on biotechnology.

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