

NIH wins patent on basic technique covering all *ex vivo* gene therapy

Washington. W. French Anderson, one of the pioneers of gene therapy, is at the centre of a new controversy following the announcement last week that the National Institutes of Health (NIH) have been awarded a broad patent covering one of the basic techniques in the field.

The patent, on which Anderson is the first named inventor (the other two are Steven Rosenberg and Michael Blaese), covers all *ex vivo* manipulations in which malfunctioning human cells are genetically altered to produce therapeutic levels of protein outside the body and then replaced.

Although the patent does not cover the alternative technique of *in vivo* manipulation — and is restricted to the United States — it is still sufficiently broad to have generated widespread comment. “Deep disbelief, I’d say that’s what most people feel about the breadth of the patent,” says Joseph Glorioso, head of the department of molecular genetics and biochemistry at the University of Pittsburgh. “This is analogous to giving someone a patent for heart transplants.”

The patent is based on the first human gene therapy trial, carried out in 1990 by Anderson, Rosenberg and Blaese, all then at the NIH, and involving the treatment of a child with the rare blood disorder adenosine deaminase deficiency. “What we did was to provide proof in principle that gene therapy can work in humans,” says Anderson. Since then, the technique is being developed as a potential treatment for disorder ranging from cancer to AIDS.

Since 1988, Anderson’s work at the NIH has been co-sponsored under a Cooperative Research and Development Agreement (CRADA) by Genetic Therapy Inc. (GTI) in Gaithersburg, Maryland. As a result, the company now has an exclusive licence for

the technology involved, and anyone commercializing an *ex vivo* gene therapy in the United States must negotiate a sublicense from the company.

Most research is exempt from this requirement. Even so, says Glorioso, the exclusive licence gives GTI considerable power. “They will be able to pick and chose winners in a very young field, and therefore to shape its development.”

Anderson, who since 1991 has chaired GTI’s board of scientific advisers, acknowledges that in principle this is true. But he points out that the US government, through the NIH, owns the patent, and that the company’s licence is granted under a CRADA, which should ensure that it is made widely available.

Other patents are also pending. At the end of last week, Anderson and three colleagues from the University of Southern California in Los Angeles, where he now works, filed an application covering their *in vivo* gene therapy, although it is more narrowly focused than the patent just granted.

The patent granted last week, broad as it may be, is less wide-ranging than the original application, filed in 1989. That was for all gene therapy techniques, both *ex vivo* and *in vivo*. But, as frequently happens, this was whittled down by the US Patent Office. The last concession made by the applicants was to exclude the expression of marker proteins. Anderson says he accepted that concession — once GTI’s lawyer had silenced his protests with a kick under the table.

But the company itself recognizes that the breadth of the patent could provoke a challenge. If so, a crucial set of documents will be the so-called ‘file wrapper’ containing the history of GTI’s negotiations with the Patent Office. These will show whether the

claim is as broad as it appears to be, and whether there are grounds for a challenge.

One lawyer who is already studying the dossier closely is Albert P. Halluin, a partner at Penney & Edmonds in Menlo Park, California. Halluin is an attorney for the company Somatics, based in Seattle, which was



Anderson: provided first working proof.

formed on the basis of a patent issued to the Whitehead Institute in Cambridge for *ex vivo* gene therapy with epithelial cells.

There is widespread speculation that Somatics may challenge GTI’s patent. But Halluin says merely that he is trying to get a better understanding of the claim. As for what happens now to gene therapy and patents, he says: “We are all playing poker, and this is the first card turned up.”

Given such uncertainty, there is no clear road map. Many leading participants, however such as Robert Abbott, president and chief executive of the gene therapy company Viagene, based in California, see a general shift from *ex vivo* to *in vivo* techniques.

All the current research in Anderson’s laboratory, for example, is now *in vivo*. But *ex vivo* gene therapy is likely to remain important, even when *in vivo* techniques are developed. It may be some time before these are sufficiently advanced for companies to seek approval for therapies from the Food and Drug Administration.

Meanwhile, there is widespread acknowledgment that the patent is the first concrete evidence of an important shift in policy at the US Patent Office, announced last December, whereby patent examiners no longer demand extensive proof of the utility of an invention before issuing a patent.

Such a demand has been difficult for gene therapy researchers to meet, as the field is only now moving to efficacy trials. Uncertainty about whether patents would be granted has contributed to the recent reluctance among venture capitalists to invest in biotechnology companies.

“The patent office recognized the creativeness in this [*ex vivo* gene therapy] concept before the proof of efficacy, and that is good,” says Jim Wilson, director of the Institute for Human Gene Therapy at the University of Pennsylvania, adding that the patent office’s policy shift office will help attract some much needed capital into the biotechnology industry. **Helen Gavaghan**

Joseph Needham, embryologist and historian

London. **Joseph Needham, the first director of national sciences.**

biochemist and embryologist best known for his multi-volume work on the history of Chinese science, has died in Cambridge aged 94.

Appointed a fellow of Caius College Cambridge in 1924, Needham later succeeded J. B. S. Haldane as a university reader in biochemistry. His interest in Chinese science developed in the 1930s and 1940s, and after the war he became Unesco’s

The first volume of his mammoth

***Science and Civilization in China*, a systematic overview that has occupied a growing team of historians of science and technology, appeared in 1954. The latest volume and the last to be directly supervised by Needham — on “missiles and sieges” — was published by Cambridge University Press earlier this month.** □

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