Genetic engineering patents

Contest in prospect over interferon rights

Washington

BATTLE lines are now being drawn up in what may be the first major contest for patent rights over a commercially significant product of genetic engineering.

The product, human leukocyte (alpha) interferon, has shown potential in clinical trials against some cancers and viral diseases, including the common cold. Last year Biogen NV of Cambridge, Massachusetts, and Geneva, Switzerland, announced it had received a European product patent for alpha interferons produced by recombinant DNA techniques; the company expects shortly to be issued with a US patent covering the same claims. Now, however, Hoffman-LaRoche Inc. of Nutley, New Jersey, has announced that it has received a US patent covering "all highly pure human leukocyte interferons no matter how they are made". John Saxe, chief patent counsel for Roche, says the company is "not aware of any highly pure leukocyte interferon product that does not fall within the issued claims". Schering-Plough Corporation, which produces Biogen's interferon (trademarked Intron) under licence, immediately challenged Saxe's claim, denying that Intron fell within the scope of Roche's patent.

The Roche patent is based on the 1970s work of Sidney Pestka and Menachem Rubinstein, in which they isolated and purified alpha interferons from human cells. LaRoche expects to receive a further US patent covering its own recombinant alpha interferon, Roferon-A, which was developed in collaboration with Genentech Inc. of San Francisco. The patent already issued to Roche defines interferon by its anticytopathic activity as assayed by two standard cell lines but does not include sequence data; Biogen's European patent, in contrast, does specify the product by sequence. A further complication is that Biogen's patent, which was filed before that of Genentech/Roche, strictly refers to an interferon precursor molecule, not the mature molecule, according to Genentech.

Alpha interferon is undergoing clinical trials at several centres in the United States. Diseases in which it has shown potential include Kaposi's sarcoma (often associated with acquired immune deficiency syndrome), multiple myeloma, malignant melanoma and hairy cell leukaemia. Both Schering-Plough and Roche have submitted marketing applications to the Food and Drug Administration for their respective products, which differ by a single amino-acid residue. Schering's Intron is approved for use in two indications in Ireland and the Philippines.

The courts have yet to test patent law as applied to genetic engineering products, and many small companies are seriously concerned that their product options might be constrained by broad product patents. Both Schering-Plough and Roche, as major corporations, have the resources to endure a court battle should one become necessary: Peter Feinstein of Biogen says he is confident that Schering will be able to prevent Roche from marketing Roferon-A. But industry analysts point out that large pharmaceutical corporations tend to avoid court cases wherever possible, and some sort of compromise may yet be negotiated.

Whatever the resolution of the present dispute, it is unlikely to serve as a model for future cases; with each product patent issued, the extent of "prior art" increases and future patents become harder to defend. One possible pointer to the future, however, is the recent US patent granted to Cetus Corporation covering what it calls muteins of interleukin-2, a lymphokine with anticancer and antiviral potential. The muteins are specific modifications of the natural protein: the Cetus mutein is claimed to be more stable than natural interleukin-2. Just as important, however, Cetus is confident that its mutein will lie outside the scope of other interleukin-2 patents.

Tim Beardsley

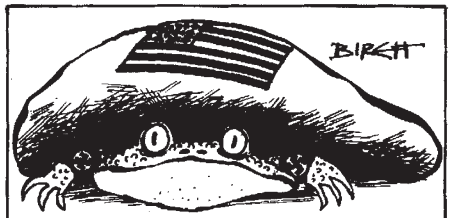
Military manoeuvres

Scientists' Nazi past laundered

Washington

US ARMY intelligence officers deliberately altered the dossiers of German scientists brought to the United States at the end of the Second World War to conceal their Nazi party activities and, in some cases, even their indictments for war crimes. Government documents released for the first time leave little doubt that the Army's intention was to circumvent President Truman's order that no "active supporter of Nazism or militarism" be allowed into the country under the programme of recruiting German "specialists".

Among those whose dossiers were altered was Wernher von Braun, the rocket scientist who later assumed a leading role



in the US space programme. Von Braun's original dossier labelled him a "potential security threat".

The Army also attempted to recruit four scientists who were later indicted at Nuremberg for war crimes. One was sentenced to 20 years' imprisonment for participating in experiments in which concentration camp inmates were forced to drink sea water.

The documents, which are the first to show a deliberate cover-up by the Army, were obtained by a reporter for the *Bulletin of the Atomic Scientists* under the Freedom of Information Act. A full account will appear in the April issue of the *Bulletin*.

Under President Truman's order, the State Department had to pass on scientists recruited by the Army. In early 1947, the State Department refused visas for several scientists labelled in security reports as "ardent Nazis". The director of the recruitment programme, Bosquet Wev, then complained to the Army's intelligence director that "the best interests of the United States have been subjugated to the efforts expended in 'beating a dead Nazi horse'". Wev said "the most positive and drastic action" was needed. The most revealing document came later that year: Wev again wrote to Army intelligence, and enclosed dossiers of 14 scientists, including von Braun: "...security reports recently forwarded from your headquarters classify 14 specialists as potential or actual threats to the security of the United States...there is very little possibility that the State and Justice Departments will agree to immigrate any specialist who has been classified as a...security threat...It is requested that the cases of the specialists listed in paragraph one be reviewed and that new security reports be submitted where such action is deemed appropriate in view of the information submitted in this letter." All were subsequently changed.

Other dossiers — such as those of the scientists indicted at Nuremberg — appear to have been "clean" from the start. The dossier of Arthur Rudolph, the NASA scientist who left the United States last year to avoid being deported for his role in the persecution of slave labourers at the V-2 rocket plant that he managed during the war, made no mention of evidence from the Nuremberg trials implicating Rudolph nor of his having joined the Nazi party in 1931.

All told, 765 scientists and technicians were recruited under the programme. The documents confirm that a major concern of the US officials who ran the programme was not letting the German scientists fall into Soviet hands. Wev wrote in one memorandum: "The return of these scientists to Germany would present a far greater security threat to the United States than their retention in this country".

Stephen Budiansky