Switzerland

Engineered *E. coli* produce interferon

THE announcement, last week, by Professor Charles Weissmann of the University of Zurich that his laboratory, on behalf of Biogen, had managed to recover biologically active interferon from bacteria containing human interferon DNA, establishes Biogen as a company that means business. Although the yield of interferon so far obtained from the genetically engineered bacteria is far too low for commercial production, Professor Weissmann thinks that "if things work out as hoped, we should have a high yielding strain within six to twelve months and we could then move relatively fast".

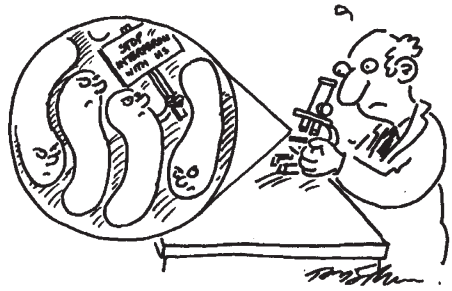
Until recently interferon has only been available in very small quantities with a purity of less than 1%. It has been produced by laboriously purifying human lymphocytes taken from blood donated for transfusion in Finland. A number of very small scale clinical trials have suggested that interferon is effective not only as an antiviral agent but also in the treatment of neoplastic disease. Because of the success of the initial trials there is now a tremendous demand for sufficient interferon to set up bigger trials.

The man behind the Finnish programme is Dr Kari Cantell. He provided Biogen with the human lymphocytes from which its genetic engineering approach started. The first step in that approach was to prepare complementary single stranded DNA from a crude mixture of messenger RNA extracted from virus-stimulated human lymphocytes.

Since there was no way to isolate the sequences corresponding to the interferon gene from the DNA, it was necessary to clone the DNA at random (using the plasmid pBR322 as vector and *Escherichia coli* as the bacterial host) and then to screen the resultant bacteria for any that contained the interferon gene.

Five thousand bacterial clones were screened by extracting their plasmid DNA. The plasmids containing interferon DNA were determined from their ability to direct the production of biologically active interferon when injected into oocytes of a frog. Having identified individual bacterial clones containing interferon genes, Professor Weissmann's team established that the bacteria were producing interferon with much the same biological and chemical characteristics as authentic human lymphocyte interferon.

It remains to be seen whether the bacteria can be further manipulated to



increase their yield of interferon, currently running at one thousand fold less than that produced from an equivalent culture volume of human lymphocytes. Professor Weissmann is confident that that can be done. He is somewhat more concerned about the potential clinical activity of bacterially produced interferon, since it is unlikely that bacteria can add the carbohydrate chains that are naturally present on the protein molecule. Current indications, however, are that this will not matter clinically.

If the carbohydrate groups do turn out to improve clinical activity, genetic engineering will probably be a less profitable route to interferon than the alternative approach of cell culture, which is already producing enough interferon for some clinical trials. For example, the Wellcome Research Laboratory in Beckenham, UK already extracts interferon from virus-transformed lymphoblastoid cells in sufficient quantities to satisfy a UK Medical Research Council sponsored trial in myelomatosis. Many, perhaps dozens, of other laboratories are undertaking a similar approach although some of them, such as Searle Laboratories in High Wycombe, UK, use fibroblasts rather than lymphoblastoid cells.

Biogen is not alone in its genetic engineering approach to interferon. Amongst other industrial concerns, some of them with an undeclared stake in the business, Searle Laboratories and the Dupont Chemical Co (in Wilmington, Delaware) are thought to be particularly close on Biogen's tail. Dupont in collaboration with the California Institute of Technology has recently sequenced one end of interferon. They will now probably synthesise the complementary DNA sequence and use it to fish out bacterial clones that contain interferon genes.

What must already concern Biogen's industrial competitors is the patents that Schering-Plough have applied for on behalf of Biogen in which they hold 15% of the shares. Professor Weissmann says that the patents are connected with the plasmid rather than the process and no one knows whether they will be granted. In any case, most of the eventual profits that accrue from interferon or any other Biogen product will finish up in the US, a fact which does not please Professor Wiessmann, himself a shareholder.

It is a great pity, he told *Nature*, that none of the Swiss or German companies that were originally approached was willing to take a major share in Biogen. The more the pity because several eminent European scientists are attached to the company and because its own laboratories are in Geneva. These are already occupied by the first recruits and a director of research is being sought. The interferon work has been carried out during the last 18 months in Professor Weissmann's own laboratory but was paid for by Biogen.

Peter Newmark

United States

Registration proposed for private DNA research

A bill that would require companies to register details of their research and production activitities involving the use of recombinant DNA techniques is to be introduced into the US Senate by Senator Adlai Stevenson, chairman of the Science, Technology and Space Subcommittee.

The proposed bill, which Senator Stevenson refers to as a "reasonable alternative" to comprehensive regulation, would cover individuals and institutions not presently required to observe the National Institutes of Health's safety guidelines. The Secretary of Health, Education and Welfare would have to be notified of all research, development and production activities using these techniques — including the source of the DNA, the type of hostvector system used, and the volume of growth media — with a civil penalty for non-compliance.

The bill also includes procedures to guarantee the protection of trade secrets. And to provide an opportunity to evaluate claims of voluntary compliance with the NIH guidelines, it would also require the secretary of HEW to report annually to Congress on the adequacy of safety precautions reported to have been taken.

Senator Stevenson is proposing to schedule hearings within the near future on the status of current regulation and development of recombinant DNA research. How far the bill goes, however, will depend partly on the support that it gets from Senator Edward Kennedy's Human Resources Subcommittee, which has jurisdiction over medical research — and with the presidential campaign now in full swing, the subcommittee is not expected to give the bill high priority.

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