

Gene transfer to humans approved in face of advice

- Data not made available to expert committee
- Lymphocytes to be tracked in cancer patients

Washington

THE Recombinant DNA Advisory Committee (RAC) of the US National Institutes of Health (NIH) has approved an experiment to introduce lymphocytes containing a bacterial gene into terminally ill cancer patients. The RAC approved the experiment at a meeting on 3 October, despite the fact that an RAC subcommittee on human gene therapy had voted unanimously four days earlier to defer approval until it received additional details about the experiment. The details were provided on the day the full RAC met.

The proposed experiment was first submitted to the RAC in June (see *Nature* 333, 697; 1988). It is a joint effort between the laboratories of W. French Anderson of the National Heart Lung and Blood Institute and R. Michael Blaese and Steven A. Rosenberg of the National Cancer Institute. The experiment is intended to track lymphocytes isolated from cancer tumours which are stimulated with interleukin-2, grown in culture and then reinjected into the patient with additional interleukin-2. These tumour-infiltrating lymphocytes (TIL) cells have anti-tumour activity, and when activated can cause remarkable shrinking of some tumours.

To track TIL cells, researchers plan to insert a marker gene — in this case the gene for neomycin resistance — into the TIL cells using a retrovirus incapable of replicating itself, so that once the TIL cells are infected, no further retrovirus is produced. It will then be possible to look for evidence of the activated TIL cells in the target tumour weeks after they are injected into patients. Conventional radio labels are either too short-lived or too toxic to do the job.

The RAC referred the original proposal to its human gene therapy subcommittee, which met on 29 July. At that time, the subcommittee recommended deferring approval until several points had been cleared up. In particular, the subcommittee sought proof that a suitable mouse model for the protocol existed and that there was adequate reason to believe that the technique would insert the marker gene into the desired cell. The subcommittee also wanted reassurance that it would be possible to demonstrate that the retrovirus vector was not somehow reproducing in the patient's body.

Anderson, Rosenberg and Blaese responded to the subcommittee in a letter dated 9 September. Although it dealt with

many of the issues, the letter failed to present data that the subcommittee felt addressed their questions. On 29 September, the subcommittee held a one-hour conference call involving 10 of the 14 subcommittee members as well as three consultants. They concluded that "although some progress has been made, we [are] not yet in possession of the requested information", and recommended that the full RAC defer approval.

It therefore came as a surprise when on Monday, 3 October, Anderson appeared before the full RAC with the data the subcommittee had been requesting. Anderson says that he withheld a written response to the subcommittee because he believed that providing the material would place it in the public domain, so that it could then be published in a newspaper or other publication not subject to peer review. Anderson says that, following consultations with the editors of *Science* and *New England Journal of Medicine*, he decided that this could jeopardize publication of papers concerning this work in these journals.

Both Daniel Koshland, editor of *Science*, and Arnold Relman, editor-in-chief of *New England Journal*, agree that prior publication of data can jeopardize publication in their journals, but both felt that this was unlikely in the present circumstances. Koshland and Relman also say they would never suggest that Anderson withhold data from a legitimate government body.

Paul Neiman of the Fred Hutchinson Cancer Research Center in Seattle and a member of the subcommittee, says he felt it was inappropriate to ask the RAC to make a scientific judgement about Anderson's data without time to study them. His impression of what was presented was that it did address many of the points on which the subcommittee was seeking clarification.

Anderson says he knew that the subcommittee would be upset to learn that some of the data they were seeking were indeed available. But he insists that some experiments, including those showing that the neomycin-resistant gene could be introduced into murine TIL cells, were only completed a week before the RAC committee met.

The experiment must still be approved by the Institutional Review Boards of the two NIH institutes involved, and James Wyngaarden, director of NIH, must give his formal approval.

In addition, the Food and Drug Administration (FDA) must give its approval for the process of retroviral mediated gene transfer. The application to FDA was submitted last week. Ten patients whose cancers have not responded to conventional therapies will be the first involved in the protocol.

Joseph Palca

India plans international astronomy centre

New Delhi

ASTRONOMY teaching and research at Indian universities will benefit from plans to set up an inter-university centre for astronomy and astrophysics (IUCAA) at Pune, near Bombay. One of the main objectives of the national facility will be the development of trained manpower, and the centre will be directed by the well-known astrophysicist Jayant Narlikar.

Because only a handful of universities offer instruction in astronomy, India is facing a tremendous shortage of astronomers, says Narlikar. The subject has been neglected primarily because all existing astronomical facilities in India are located outside universities, at national observatories. The absence of a close link between the observatories and the university community has meant that even motivated students are deflected away from making astronomy their career.

The centre, set up by the University Grants Commission, will have a core of 20 leading astronomers, who will participate in research and administer the centre's

graduate school, which will be open to students from all Indian universities. The research and training activities of the centre will revolve around the giant metre-wavelength radio telescope being built about 100 kilometres from Pune.

Besides the in-house teaching programme, Narlikar says that IUCAA will promote astronomy programmes at selected universities by sending its staff on lecture tours and by sponsoring research projects. It will also run an associateship programme similar to that of the International Centre for Theoretical Physics at Trieste, Italy. The university community will be allowed access to the centre's instruments, data centre, library and computer, and the centre will help university academics to obtain observing time at observatories in India and abroad, and to develop payloads for space astronomy.

According to Narlikar, IUCAA "could very well expand its role and be a focal point for research in astronomy and astrophysics for the Afro-Asian region as a whole".

K.S. Jayaraman