

Assumptions of AIDS inquiry challenged

- Meaning of viral similarity questioned
- Contamination blunts effect of new results

London & Washington

AS the National Institutes of Health (NIH) inquiry into the part played by Robert Gallo's laboratory in the discovery of the AIDS virus enters its tenth month, astonishing new evidence has appeared in print that strikes at the central assumption behind allegations of misconduct.

Studies published in the August issue of the *Journal of Virology* imply that two groups of researchers have isolated almost identical strains of human immunodeficiency virus (HIV) from two totally unrelated patients — a finding that could undermine allegations that the close similarity between the virus isolated by Gallo's laboratory at the US National Cancer Institute and that discovered at the Pasteur Institute in Paris by Luc Montagnier must mean that Gallo's virus ultimately came from samples provided by Montagnier.

A race is now on to check the new results, with hectic efforts being made to trace the patients from whom the original samples were taken. Although a final verdict is unlikely before the end of the month, there are grounds for believing that the new results must at this stage be assessed agnostically. In particular, it is possible that both isolates are actually laboratory contaminants of the original French virus. If that proves to be the case, their similarity would be further evidence of the ease with which HIV can spread accidentally in the laboratory.

The viruses were characterized by David Volsky's group at Columbia University in New York and Mario Stevenson's laboratory at Nebraska University. As reported, they come from two independent isolates, one obtained in 1984 from an AIDS patient in New York,

ASTRONOMY

Mt Graham go ahead

Washington

AFTER two years of court battles, protests and federal investigations, Arizona's Mount Graham may finally have a telescope. The US Forest Service announced at the end of last month that US conservation law does not require further studies of the project and issued a building permit on 24 August. Construction of the first of three telescopes on the 10,700-foot peak, which is the only home of the endangered Mount Graham red squirrel, will begin within weeks, according to a spokesman at the University of Arizona.

Christopher Anderson

the other from a seropositive haemophilia patient in Nebraska in 1989. An analysis by Gerald Meyers of the HIV sequence database at Los Alamos (see News and Views page 18), shows that they differ by less than 2 per cent. This finding jars with the conventional view that viral isolates from different individuals, or even the same individual at different times, are bound to display marked genetic differences.

Significantly, the sequences are not only conspicuously similar to each other, but also to those of two other isolates, LAV1 and HTLV-IIIIB — the names given to the original viruses discovered by Montagnier and Gallo in 1983 and 1984 respectively.

The panel conducting the inquiry at NIH's Office of Scientific Integrity (OSI) has spent much of the summer quizzing AIDS researchers and poring over notebooks from Gallo's laboratory. High on their agenda has been the issue of whether or not viruses as similar as HTLV-IIIIB and LAV1 can emerge from two unrelated patients. On the face of it, the genetic sequences reported in the *Journal of Virology* articles say that they can.

Deputy OSI director Suzanne Hadley says that the inquiry panel is well aware of the implications of the sequences, but added that, although the genetic similarity of different HIV isolates "is an important issue, it's not the only issue". When asked if the panel would be commissioning an independent study to verify the sequences, she said, "That kind of analysis may be an interesting thing to do. There's no area closed."

But there are signs that the new sequences may not be quite what they seem. In particular, a process of contamination cannot be ruled out, especially because Stevenson worked as a postdoctoral researcher in Volsky's laboratory at the University of Nebraska. Before Volsky moved to New York in 1987, he helped to establish the cell line used to grow the viral isolate from the New York patient, termed N1. It was from this cell line that, in December 1984, Volsky derived the cloned virus N1T, which he used in later biological studies and finally sequenced.

The virus sequenced by Stevenson's group in 1989 is known as MFA. According to their *Journal of Virology* paper, it was derived from an isolate called MF, which was originally obtained from a clinic in Nebraska. Nonetheless, when asked about the possibility of contamination, Stevenson made this statement: "We

maintain the source of the original N1T isolate, N1-infected CEM cells, in our laboratory, and have cited that cell line whenever we've used it. Given the similarity of the MFA and N1T sequences to HXB2 (HTLV-IIIIB) and BRU (LAV), I must accept the possibility that the MF isolate was in fact derived from cultures contaminated with N1-CEM cells."

But even if Stevenson's MF virus does come from a contaminant, the remarkable similarity between Volsky's N1 isolate and LAV1 remains. Could the cells used by Volsky's laboratory to culture the original N1 isolate somehow have become contaminated with LAV1?

Volsky says that between 1984 and 1985 his laboratory prepared about 1,000 different viral cultures using only HIV-infected serum from a clinic in New York. During the autumn of 1984, however, he says that the original cells containing the N1 isolate were co-cultivated with CEM cells donated by Montagnier's laboratory.

Volsky has maintained that, to the best of his knowledge, these were virus-free and would have been routinely checked for signs of virus before being added to N1 cultures. But Montagnier's laboratory records suggest that, in 1984, he sent Volsky LAV1-infected CEM cells, in addition to any virus-free cells of which there is no specific mention in the records. "He asked for LAV-infected cells, and we gave him those", says Montagnier.

Although Volsky cannot recall receiving LAV1-infected cells, he admits that in the light of Montagnier's record they were probably sent. "If we received contaminated CEM cells harbouring latent virus that became reactivated during co-culture, there is nothing one can do", says Volsky.

Regardless of whether infected cells were actually received, Volsky stresses that an active culture producing LAV1 was never established in his laboratory.

William Blattner, an epidemiologist at the National Cancer Institute, has been searching for Stevenson's patient so as to resequence the virus. Although he has no name for the patient — nor does he know if he or she is still alive — the number of possible candidates has been narrowed to 20 or 30, he says.

By contrast, Volsky's patient has been traced and is still alive. Since virus was first isolated from him in 1984, he has become seronegative by the standard antibody test. Nevertheless, Volsky's group has managed to detect HIV genetic material in his blood and now plans to sequence it. They also intend to sequence DNA from frozen samples of the N1 isolate obtained in 1984. The sequencing should be completed by December, says Volsky, who believes that final judgment on the origin of the similarity of N1T and LAV1 should be reserved until then.

David Concar & Christopher Anderson