

Gallo Challenged on HIV Isolates

With a paper published 2 weeks ago in *Nature*, Robert C. Gallo of the National Cancer Institute thought he had nailed down one element in the contentious history of the AIDS virus. So did *The Washington Post* and *Newsweek*: each suggested that Gallo may have exonerated himself from any possibility that he had intentionally or inadvertently taken the isolate of France's Luc Montagnier as his own. But rather than clearing up the issue, Gallo's critics say, this latest report raises yet more questions about the origins of the now infamous isolate. And, in an embarrassing side issue, Gallo and his coauthors have had to admit that two of the three figures in the report contain errors that will require a correction.

Gallo hoped his paper would lay to rest accusations that have arisen from the troublesome discovery that the virus that Gallo isolated in 1983 and called HTLV-IIIB was genetically nearly identical to the one called LAV-1 that Montagnier had isolated earlier at the Pasteur Institute. That question has been explored at length by investigative journalist John Crewdson of *The Chicago Tribune* who, in a major article published in 1989, raised the possibility that Gallo had misappropriated Montagnier's vi-

rus. To lay such allegations to rest, Gallo went back to his freezers to retrieve samples of a virus Montagnier sent him from an AIDS patient known as BRU in 1983. Only if the samples of virus from BRU were identical to HTLV-IIIB would the accusations hold water.

Much to the delight of Gallo and his supporters, the viruses appeared very different. According to Gallo's published report (*Nature*, 28 February, p. 745), unlike HTLV-IIIB, BRU would not grow in special T-cell lines hospitable to the AIDS virus, and the DNA sequences of the two viruses differed by about 10%. Although these results did not explain the genetic similarity between HTLV-IIIB and LAV-1, they did appear to rule out the possibility that the 1983 BRU samples Montagnier sent Gallo were the source of HTLV-IIIB. Indeed, now an intriguing new question might be posed: Where did LAV-1 come from? Montagnier has maintained all along that LAV-1 came from BRU. But Gallo's data showed that the 1983 BRU samples he received differed as much from LAV-1 as they did from HTLV-IIIB. Could LAV-1 have been a contaminant of Gallo's isolate?

Enter Gerald Myers, keeper of the AIDS

virus database at Los Alamos National Laboratory. Myers told *Science* that there is a problem with Gallo's analysis of the molecular differences between BRU and LAV-1/HTLV-IIIB. To compare two viral sequences, researchers use a computer algorithm to align the sequences and then count the number of mismatches. But often there are gaps in the sequence of one of the viruses. Myers says these gaps are ignored when researchers compare sequences, but Gallo and his associates counted each base pair in the gap as a mismatch. The result, says Myers, is an inflated impression of how different the viruses are.

"Nobody does that," he says, "and it's leading to widespread misunderstanding...that these sequences are very different." In fact, Myers says, the published BRU sequences "are the closest sequences to IIIB and LAV-1 that we're aware of." Properly calculated, the difference is about 5%. Myers also points out that the sequences published in figures 1 and 2 in the *Nature* paper contain between 14 and 20 typographical errors compared to the sequences submitted to his database electronically.

Marvin S. Reitz, one of Gallo's colleagues who coauthored the *Nature* correspondence, concedes that the figures contain errors, and says a correction is being prepared. He also agrees that his method of calculating percent similarity may not be standard. But both he and Gallo say this does not change the paper's basic conclusion: that the 1983 BRU isolates and HTLV-IIIB are two different viruses. "In my opinion, looking at those sequences, they seem to be too different to have come from the same patient," says Reitz. Gallo is even more emphatic. "Serologically, biologically, and molecularly," the viruses are different, he insists, adding that the *Nature* report is nearly unassailable proof that the 1983 BRU virus could not possibly be from the same person as HTLV-IIIB/LAV-1. "In my view, it means strongly that he [Montagnier] had a contamination some time in 1984. It doesn't mean the contamination came from our lab, and it doesn't mean the contamination came from us to them."

"I'm not saying that these sequences came for sure from the same patient, but if they came from different patients, one would have expected them to be more different than they are," says Myers. Who is right? The French are feverishly analyzing additional BRU isolates, and *Science* has learned that NIH is hoping to do this as well. Molecular biologist Simon Wain-Hobson of the Pasteur Institute says "We'll reply when we have the data, and we'll do it properly."

■ JOSEPH PALCA

With reporting by Jeremy Cherfas.

NCI Collaborations Suspended

The National Institutes of Health recently rescinded permission for Robert C. Gallo and several other researchers at the National Cancer Institute to collaborate with three foreign institutions, one in France and two in Zaire. The move, which was first reported in *The Chicago Tribune*, follows an investigation by NIH's Office of Protection from Research Risks (OPRR) into the nature of collaborations between NCI scientists and Daniel Zagury of the Université Pierre et Marie Curie in Paris, who conducted tests of an AIDS vaccine in Zaire. An OPRR memorandum on the matter obtained by *Science* concludes that the NCI scientists had failed "to provide and document adequate protections for human subjects in international collaborative research." Researchers who have heard about the memorandum are worried that the incident may have a chilling effect on international collaborations at NIH.

OPRR began its investigation after NIH received a letter last summer from *Tribune* reporter John Crewdson alleging, among other things, that Zagury conducted his experiments on young children without appropriate approval from French and Zairan ethics committees, and that Gallo and others had failed to receive appropriate permission to collaborate with Zagury or to provide him with materials for his work.

A spokesman for NIH denies the *Tribune* story's claim that Gallo has been barred "from continuing human subject research with any other foreign scientists," saying rather that the permission for continuing this particular collaboration has been rescinded.

Whatever the current NIH reaction may mean to Gallo, several researchers contacted by *Science* said they will now be far more careful in complying with paperwork requirements for international collaborations, and they worry that this could bog down the review processes. Phil Chandra, director of the Fogarty International Center at NIH, admits that "if it turns out that a lot of people are not following the rules, there could be a problem." ■ J.P.