# The True Source of HIV?

*The Pasteur Institute may have pinned down the origins of their first viral isolate. Will that end years of acrimony?*

FIRST *TWIN PEAKS* WENT OFF THE AIR, THEN "Dallas" got the ax, and now one of science's longest-running soap operas may also be drawing to a close. If the findings of a report to be published later this month in *Science* hold up, Luc Montagnier and his colleagues at the Pasteur Institute in Paris may have finally identified the true source of an AIDS virus strain that has been the focus of a bitter dispute between their group and a group led by Robert C. Gallo at the U.S. National Cancer Institute (NCI). The Pasteur researchers' report should end speculation that their virus might have originated in Gallo's NCI lab. And like any good soap opera, this one has a suitably bizarre twist for its ending: The source of the strain has been different from what the science world has been told for most of the past decade.

**News of the apparent dénouement first appeared in the 5 May edition of the *Chicago Tribune*, which had obtained an unedited draft of Montagnier's paper. As a result, *Science* took the unusual step of lifting its embargo policy the following day to allow other reporters access to the corrected paper. The paper is scheduled for publication on 17 May.**

The years of drama have focused on why a Pasteur isolate known as LAV was virtually identical to another isolate—dubbed HTLV-IIIB—that was grown in cell culture by Gallo's group. At first, that question had legal and financial implications: Both HTLV-IIIB and LAV were used to make commercial AIDS blood tests, which have grossed millions of dollars in worldwide sales. But a settlement between the U.S. and French governments was signed in 1987, stopping legal action. As a result, both sides agreed to share the credit and royalties from the discovery.

Still, scientific questions about the origins of HTLV-IIIB/LAV persisted. The French lawsuit was based largely on the fact that Montagnier had sent Gallo samples of a virus he had isolated from an AIDS patient with the code name BRU early in 1983. When it later became clear that LAV—which the French group said was derived from BRU—and HTLV-IIIB were genetically identical, allegations began flying that Gallo had deliberately or inadvertently grown the French virus and claimed it as his own. The NIH Office of Scientific Integrity opened an investigation only to conclude last fall that Gallo had many other isolates and therefore had no apparent motive for consciously taking the French isolate. But the soaper didn't end there: NIH continued its investigation into possible misconduct involving some of the early papers from Gallo's lab.

Meanwhile, in February of this year, matters took an unexpected turn. Gallo and his colleagues reported in *Nature* that three of the five samples the French had sent him in 1983 had sequences that differed from the published sequence of LAV (*Science,* 15 March, p. 1306). If Gallo was right, BRU couldn't be the source of either LAV or HTLV-IIIB. That raised the possibility that Gallo's virus may have contaminated the French lab.

The Pasteur scientists were stunned. They went back to their lab notebooks and reanalyzed samples of BRU stored in their freezer. To their surprise, they found that Gallo was indeed correct. The early samples of BRU lacked a telltale feature that distinguishes HTLV-IIIB/LAV from all other isolates sequenced to date: a peculiar amino acid sequence in the so-called V3 loop, a portion of the protein envelope that surrounds the virus.

So if LAV wasn't BRU, what was it? Montagnier and his colleagues quickly found the answer. As will be described in their forthcoming paper, another isolate growing in the Pasteur lab in 1983, from a patient code-named LAI, did have the characteristic sequence in the V3 loop. The Pasteur researchers determined that sometime during a 2-week period at the end of July 1983, culture flasks containing BRU virus were being handled along with flasks containing LAI virus, and cross contamination occurred. Pasteur virologist Simon Wain-Hobson calls LAI "a rapid high virus," that is, it has the unusual property of growing well in established T-cell lines, whereas most HIV, including BRU, will only grow in recently drawn white blood cells. Because it is a fast grower, LAI quickly crowded out BRU from cultures it contaminated, and without realizing it, the French were suddenly studying a different virus.

Why weren't the Pasteur researchers surprised when their virus suddenly started growing like topsy? Wain-Hobson says that the virus only started growing well in culture after the Pasteur team had tried infecting bone marrow cells with their viral isolates. They concluded that passage through bone marrow cells might have altered the virus' characteristics. What the researchers didn't realize at the time was that this infected bone marrow sample, known as M2T-/B, was doubly infected with both BRU and LAI.

And that may explain how LAI reached the United States. Gallo acknowledges that M2T-/B arrived in his lab in September 1983, before he came up with HTLV-IIIB, but he is no longer able to find any samples of the material Montagnier sent him. (Ironically this was the virus' second visit, at least, to the United States. According to Montagnier, the young patient known as LAI most likely became infected with HIV between 1977 and 1979 while he was a student at a midwestern college. He died of AIDS in 1984.)

*Robert Gallo*

*Luc Montagnier*

Jean-Michel Vogue/Gamma-Liaison

While this latest work doesn't make explicit how LAI might have contaminated Gallo's cultures, "there is no doubt [that LAI is the source of HTLV-IIIB]," says Wain-Hobson. Montagnier told *Science* in a telephone interview that he believes LAI contamination may have occurred when Gallo associate Mikulas Popovic, in an unusual attempt to coax the AIDS virus to grow in an established T-cell line, pooled 10 different viral isolates in the hope that one of them would "take." "Probably they had LAI in the laboratory already growing" says Montagnier, "and LAI contaminated their pool, so what came up from their pool is LAI."

Gallo seems prepared to accept the French explanation. He told *Science* he has independently obtained an early isolate of LAI, and will be testing it to see if he can confirm the French results, but he already thinks this could be the final piece of the puzzle. Gallo claims it was just bad luck that he chose the LAI-contaminated HTLV-IIIB virus to develop his HIV blood test. "They had an accident, and the probability is that we had an accident," says Gallo.

Responds Montagnier: "If he agrees with that, that's it, it's finished." Stay tuned.

■ JOSEPH PALCA