

What Next in the Gallo Case?

After 2 years, the NIH investigation is drawing to a close, leaving a variety of important questions unanswered—while John Dingell calls for yet another investigation

ALMOST EXACTLY TWO YEARS AGO, ON 19 November 1989, *The Chicago Tribune* devoted a 16-page special section to investigative reporter John Crewdson and a story that has come to haunt Robert Gallo, the most prominent researcher on the intramural campus of the National Institutes of Health (NIH) and co-discoverer of the AIDS virus. After 20 months of sifting through thousands of pages of documents and interviewing more than 150 people involved in the hunt for the cause of AIDS, Crewdson focused on the fact that the virus Gallo grew in his lab and used as the basis for the AIDS blood test—a virus he called HTLV-III_B—was identical to a virus known as LAV that originated from the Paris-based Pasteur Institute. This coincidence, wrote Crewdson, was the result of either “an accident or a theft.” Once Representative John Dingell (D-MI) cited Crewdson’s exposé in a testy letter to NIH, a fact-finding inquiry by NIH’s Office of Scientific Integrity (OSI) was soon under way.

After nearly 2 full years of investigation, however, the OSI investigation appears to be on the verge of stalling out. The office still cannot answer the fundamental question raised by Crewdson: Did someone in Gallo’s laboratory steal LAV and use it to make the lucrative AIDS blood test? In fact, NIH decided not to pursue the matter vigorously in October 1990, when then acting director William Raub stated that Gallo’s lab had other viral isolates available as it was growing HTLV-III_B in quantity—a statement that was widely interpreted at the time as indicating that Gallo had no motive to steal the French virus. OSI’s sole attempt since then to address the origin of HTLV-III_B, an independent sequence analysis of viral samples used in Gallo’s early AIDS work, recently produced an equivocal report that neither proves misappropriation nor rules it out. And although sources close to the investigation argue that this report raises additional issues worth investigating, and that OSI files relevant to the sequencing report haven’t been touched “for months,” OSI appears to have concluded its active investigation in the case.

What’s more, these sources say the office is ready to back away from many of the misconduct charges it levied last summer against

former Gallo assistant Mikulas Popovic in a draft report (*Science*, 16 August, p. 728)—and that the office has reached this conclusion without the input of the three-member scientific panel that helped it write the draft report. Factor in Dingell, who has recently pressed for both a perjury investigation of Gallo and an inquiry into what his staff calls a 1986 “cover-up” of Gallo’s work with the French virus at the Department of Health and Human Services (HHS), and OSI’s attempts to close the books on this case look increasingly forlorn.

The investigation to date

By far the greatest part of OSI’s effort over the past year has been focused not on the question of misappropriation, but on suspect data in one of four seminal papers published by Gallo’s lab in *Science* on 4 May 1984. In its draft report, a copy of which *Science* has now obtained, OSI criticized Gallo’s “failings as laboratory chief and senior author of the papers” but did not conclude that these actions constituted misconduct. It did, however, state that Gallo’s former assistant Mikulas Popovic may have committed scientific misconduct for misrepresenting his work in growing a continuous culture of HTLV-III_B. In particular, the report notes that Popovic’s description of a viral “pool” that produced HTLV-III_B as “continuous” was misleading because he had twice re-fed the pool with viral samples; that the paper stated the pool samples had first been shown to test positive for reverse transcriptase, when they had not; and that Popovic had described certain experiments in a table as “not done” when in fact they had been done. Popovic, a Czech who has been in the United States since 1980, has replied that these alleged misrepresentations are either differences of scientific interpretation or a consequence of his imprecise use of English (*Science*, 16 August, p. 729).

Since completing the draft report, however, OSI has made little progress toward producing a final version. The draft was not well received by those who reviewed it, and after receiving stylistic complaints from NIH director Bernadine Healy and a panel of outside consultants, OSI decided last August to draft an “executive summary” intended to

clarify the issues in the report. But the summary is still unfinished, more than 2 months after it was commissioned. OSI deputy director Clyde Watkins, who took over the investigation after former OSI investigator Suzanne Hadley resigned from the case under pressure last July (*Science*, 26 July, p. 372), says the delay is a result of his need to familiarize himself with the details of the case. Watkins won’t predict when the summary will be done, but says he is feeling “considerable pressure” to finish it soon.

But OSI’s handling of the report and the summary has strained its relations with the three-member scientific advisory committee that has advised the investigation since last December. Watkins is writing the summary without input from panel members, although he says he intends to share it with them once it is complete. The idea, he says, is to use the summary as a “tool” that will focus the panel’s deliberations as they consider the rebuttals and decide whether or not to rewrite the draft report. But one panel member says OSI is using the summary as an “excuse” to avoid dealing with the report. “They keep saying, ‘We’re putting together an executive summary, and that’s why nothing is happening.’ But nothing is happening, and nothing keeps happening. I’m very concerned.”

NIH and congressional sources also say that Watkins and OSI director Jules Hallum are inclined to back away from several of the misconduct charges against Popovic—particularly those relating to the pool’s continuity and the reverse transcriptase tests. One source says they have been influenced by another OSI consultant on the case—Cornell retrovirologist Volker Vogt—who does not believe that Popovic’s description of the pool, for instance, warrants a charge of misconduct. According to this source, it is possible that Popovic could end up facing only one charge in the final report: that of wrongly entering into a table the notation “ND” (for “not done”) several times when the experiments had reportedly been done.

Dipping into the pool

But the final report will not focus solely on the *Science* paper. According to Watkins, it will also incorporate the results of a sequence

analysis of viral cultures from 1983 and 1984 recently completed by Roche Diagnostic Research (*Science*, 25 October, p. 507). That analysis, which *Science* has obtained, does confirm that there were seven distinct viruses in the cultures Popovic says he put in his pool in November 1983 and January 1984, and that none of them was LAV-LAI, the isolate recently determined to be the source of both LAV and HTLV-III_B. But it did little to explain when and how the pool might have been contaminated. For instance, OSI also had Roche Diagnostics test four 1984 samples of HTLV-III_B from Gallo's laboratory or its contractors. The three outside samples, dated April and May 1984, all turned out to contain LAV-LAI. The fourth, a clone known as H17 from Gallo's lab dated February 1984, contained no virus at all. As a result, an analysis that might have shown the growth of one of the original seven viruses, thereby lending weight to the contamination theory, ended up providing no evidence that any of them—or, for that matter, anything but LAV-LAI—ever grew in the pool at all.

In fact, according to a source close to the investigation, there isn't even any laboratory data that shows viral growth in the pool at all. While the *Science* paper reported 5 months of continuous reverse transcriptase production, that data apparently no longer exists. The draft report states that M.G. Sarngadharan, a third co-author of the paper, told OSI that he had not retained the data.

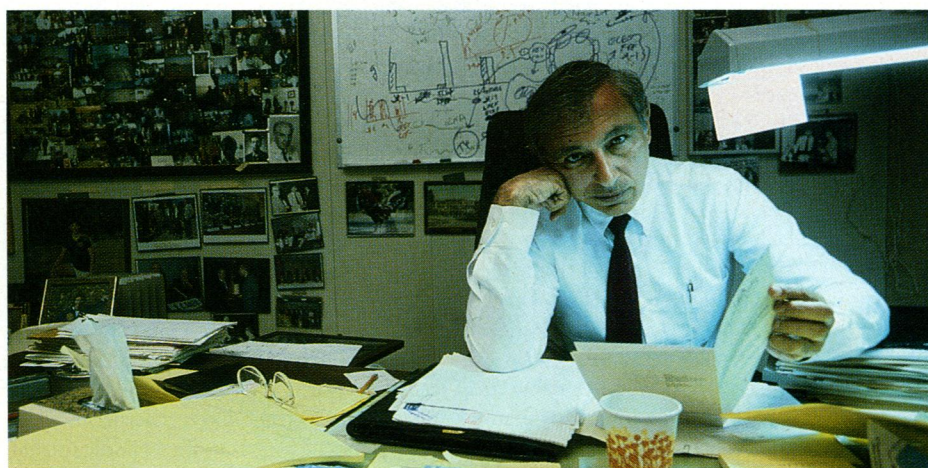
Although they will not speak for the record, members of Gallo's laboratory insist there is nothing sinister about these facts, and they maintain that an accidental LAV-LAI contamination of their cultures is the most plausible explanation for what happened to the pool. LAV-LAI, they note, has contaminated several laboratories around the world, including those at the Pasteur Institute. (LAV-LAI, in fact, was discovered just this summer to have contaminated Pasteur samples originally thought to contain Pasteur's first and most famous isolate, LAV-BRU.)

Further sequencing of the dozen or so III_B samples in Gallo's freezer could conceivably shed some light on how the pool might have been overgrown by LAV-LAI. But Watkins, who says OSI is open to analyzing any other samples, says he's unaware that any from the pool's early days still exist: "If I knew of any other samples from February [1984] or earlier, they'd be on their way to Roche Diagnostics." Another source concedes wearily that the trail may be too cold to pick up: "I think it's entirely possible that we'll never know the answer."

Coverup and conspiracy?

Even the question of misappropriation, large though it looms, could be overshadowed by events. Last week, aides to John Dingell made it known that he is interested in pursuing perjury charges against Gallo and an investigation of other NIH and Health and Human Services (HHS) officials who, Dingell contends, may have conspired to present a false history of Gallo's AIDS research during a prolonged battle in 1987 between the U.S. govern-

Popovic did "begin" growing the virus on 15 November 1983 when he started the pool, Onek adds. "What difference does it make if [Gallo] wrote November instead of December, December instead of January? He had no motive to change it by a month one way or another." NIH sources note that the Pasteur Institute applied for a U.S. patent on their blood test that December, but Onek says that the French had applied for European patents earlier yet, in September. "We get no priority for saying



Closing the books? *The OSI's investigation of Robert Gallo will soon be over.*

ment and the Pasteur Institute over patent rights to the AIDS blood test.

Dingell's staff is basing its perjury inquiry on an internal NIH memo Suzanne Hadley authored last June that challenged what Hadley called "false" and "incomplete and misleading" statements in three documents Gallo signed under oath: the blood test patent, the patent on Popovic's method for continuously producing AIDS virus in a cell line, and a sworn declaration Gallo signed on 8 November 1986 as part of the government's defense against the patent lawsuit. For instance, Gallo's declaration states that Popovic was using the cloned H9 cell line to produce virus "in relatively large amounts of a consistent composition" by November 1983. But laboratory records available to *Science* show that H9 did not exist until Popovic cloned it on 19 January 1984. Furthermore, Popovic told OSI that he had feared the pool was dying—not producing virus in "large amounts"—in December 1983.

Gallo's lawyer, Joseph Onek, says that talk of perjury is "nonsense" and dismisses the charges as "typical Hadley lies and distortions." H9 didn't exist in November, he admits—but Gallo really just meant to describe H4, an earlier cell line in which Popovic also eventually grew HTLV-III_B. And

November instead of December," he says. "Those dates are meaningless."

The point could be moot in any case, since the 5-year statute of limitations on perjury expired last Friday. Several sources, however, have noted that under certain circumstances, the statute of limitations for crimes that result in "ill-gotten gains" begins running on the date of the most recent "gain." Since Gallo has continued to receive patent royalties on a regular basis, one source says, he could still face charges. The source adds that the U.S. Attorney in Baltimore is said to be "very interested" in the case.

Meanwhile, Dingell's staff has taken aim at the higher echelons of HHS in a closely-held 100-page report they are calling "The Great AIDS Coverup." Sources describe it as a compendium of false statements on Gallo's AIDS research made by NIH and HHS officials in the period leading up to the patent fight. Dingell has called in investigators from the General Accounting Office to review these documents and the patent declaration, sources say, raising the specter of another confrontation over the patent and the unraveling of the patent settlement. If such a fight erupts, Gallo is unlikely to see the end of this controversy any time soon.

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