

HHS: Gallo Guilty of Misconduct

The verdict is that by concealing the fact that his lab put the French virus into a permanent cell line, Robert Gallo intended to mislead the scientific community

Nine months ago, Robert C. Gallo of the National Cancer Institute seemed likely to emerge from a long investigation of his work on the AIDS virus with his reputation largely intact. A report by the National Institutes of Health (NIH) had just concluded that though the eminent retrovirologist had been uncollegial in hogging credit for finding the cause of AIDS, his behavior did not constitute scientific misconduct. But last week, in a startling reversal, the Department of Health and Human Services (HHS) found Gallo guilty of misconduct for misrepresenting in a key 1984 *Science* paper the work his lab had done with a French isolate of the AIDS virus, called LAV.

Specifically, Gallo wrote in the paper that LAV had not been transmitted to a permanent cell line—even though researchers in Gallo's lab had done exactly that. The HHS report concludes that this statement shows an intent "to deceive" readers of the paper—maximizing Gallo's achievements while minimizing those of the French. HHS "censured" Gallo for several infractions that were not misconduct, including lax supervision of his lab and failure to pursue quickly the identity of the cell line in which he had grown the AIDS virus (*Science*, 22 June 1990, p. 1499). HHS also concluded—as did the NIH report—that Gallo's former chief virologist, Mikulas Popovic, had committed misconduct by falsifying results in the same paper, though HHS terms his infractions "relatively minor."

Sanctions for the pair were light. The report notes that the finding of misconduct is likely to be devastating for a scientist at Gallo's level and recommends only that his work as director of the Laboratory of Tumor Cell Biology be supervised for 3 years. Popovic, currently unemployed, is to receive the same supervision should he apply for an NIH grant. And the report argues that the finding of misconduct against Popovic should not be used to bar him from employment as a scientist.

The finding of misconduct against Gallo is not based on new information. Instead, it results from a review of the NIH report, which was written by the now-defunct Office of Scientific Integrity (OSI) and approved by NIH Director Bernadine Healy (*Science*, 8 May 1992, p. 735). The review was carried out over the past 9 months by a four-person

team at HHS's newly created Office of Research Integrity (ORI). The ORI team toughened OSI's conclusions after digesting two blistering critiques of the OSI document—one by a National Academy of Sciences (NAS) panel led by Yale biochemist Frederic Richards, the other by staffers of a congressional subcommittee chaired by Representative John Dingell (D-MI).



Reversal of fortune. Robert Gallo.

Gallo immediately released a statement blasting ORI's "new and extraordinary finding" as "utterly unwarranted," "petty," and "misguided." Gallo criticized the HHS investigation as "endless and incompetent," warning that "the mindless pursuit of fantasied misconduct can have devastating consequences for scientific research." Popovic's attorneys said in a statement that, "Instead of receiving honors for his contribution to world health, Dr. Popovic has been charged with misconduct for phrases in his paper introduced by others, a few words reflecting his lack of fluency in English, and a difference in interpretation of data."

Gallo and Popovic aren't the only ones displeased with ORI's 62-page report, which was delivered to the principals on 30 December. In fact, hardly anyone finds it completely satisfying. Gallo supporters and those involved in the OSI investigation, including

Healy, continue to argue that although Gallo was not collegial, his behavior does not rise to the level of misconduct—and that blurring uncollegiality and misconduct bodes ill for science. Gallo's critics, on the other hand, think the new report doesn't even scratch the surface of his misdeeds—in particular failing to settle the question of whether he misappropriated the French isolate.

Lyle Bivens, an experimental psychologist and ORI staffer who headed the ORI team, expected the vituperation directed at his group's report. "We knew we were going to get it no matter what we did," says Bivens. When Bivens learned last spring that he was assigned to review the OSI final report, he was far from thrilled: "If I had been given a choice I would have ducked it." He says that the other members of his team—a sociologist and two lawyers—felt the same way.

Unfortunately for the foursome, ducking the job wasn't a possibility, so they began spending long days analyzing the OSI report. According to Bivens, the team never seriously considered changing OSI's findings about Popovic, who had been charged with misrepresenting one step in one experiment, stating in two tables that some tests weren't done that actually were, and substituting a 10% value in a table for "very few cells." Bivens' team agreed with OSI that although these transgressions constitute misconduct, they did not alter the conclusions of the *Science* paper.

After reaching a consensus on the Popovic findings, however, the team decided two outstanding issues had to be resolved before they could sign off on the OSI report. One was Gallo's statement about LAV; the other was the even more explosive question of theft.

The origin of both questions lay far back in the history of AIDS research, in mid-1983, when Luc Montagnier of the Pasteur Institute in Paris was first isolating the AIDS virus, which he called LAV. Montagnier published his discovery in *Science* in May 1983, though he did not conclude then that LAV caused AIDS. Two months later, he sent Gallo's lab a sample of LAV. While still working with that sample, he received another shipment from Montagnier in September 1983. Popovic managed to get the second sample to grow in a permanent cell line. That feat—not previously achieved in any lab, in-

cluding Montagnier's—was critical, because growing the AIDS virus in a permanent cell line was a key to mass producing the virus, identifying it as the cause of AIDS, and developing a blood test. After Popovic had grown LAV in a permanent cell line, Gallo ordered him to freeze the French virus and concentrate on isolates obtained in the Gallo lab.

Those American isolates formed the basis of work reported in four landmark papers published by Gallo's group in *Science* in May 1984. Little mention was made of LAV, and there was no reference to the uses it had been put to in Gallo's lab. Indeed, the only reference to LAV was toward the end of what has become known as the "Popovic" paper, the central paper describing the isolation and continuous production of the Gallo isolates, collectively dubbed HTLV-III, from permanently growing cell lines. Popovic, Gallo, and their co-authors wrote that some apparent differences between HTLV-III and LAV might be "due to insufficient characterization of LAV because the virus has not yet been transmitted to a permanently growing cell line for true isolation and therefore has been difficult to obtain in quantity."

That statement didn't become the focus of controversy immediately, however, because it was obscured by the question of misappropriation, which arose in 1985 when the isolate Gallo used for his blood test—HTLV-IIIB—and LAV turned out to be genetic twins. The charge of misappropriation sparked a lawsuit between Pasteur and HHS, drew the attention of *Chicago Tribune* reporter John

Crewdson—as well as Dingell—and propelled the NIH investigation. OSI's investigators, however, concluded there was not enough evidence to decide whether the genetic identity between the French and American isolates resulted from accidental contamination—Gallo's explanation—or theft.

Bivens told *Science* that his team soon came to agreement with OSI on the question of misappropriation: Contamination was certainly a possibility, and there wasn't enough evidence to rule it out. But the description of LAV in the *Science* paper could not be resolved so easily, Bivens said. Gallo's defense has been that the sentence about LAV was intended only to refer to the published record at the time: It meant that the French had been unable to grow LAV in continuous culture. Since that was true, the statement could not be a misrepresentation. OSI concluded that "there is not sufficient evidence to clearly disprove Dr. Gallo's assertion of his intended meaning"—hence there could be no finding of misconduct.

Bivens' team was exposed to a less charitable perspective in two scathing critiques of the OSI report, each of which the four-person team read carefully. When the OSI draft final report was completed in January 1992, it was immediately criticized by the Richards panel, a committee of eminent scientists named by NAS to oversee the investigation and counteract any perception that NIH could not objectively investigate one of its own star researchers.

In a letter to Healy, the Richards panel took issue with OSI for faulting Popovic while

letting Gallo off the hook. In particular, the Richards letter hammered Gallo for the LAV statement, which it said was "one of the most glaring faults in the paper." Particularly damaging in the committee's view was the fact that an early draft of the paper had contained a description of Popovic's work with LAV, but these references were removed by Gallo. Not acknowledging the work with LAV, the panel thundered, constituted "intellectual recklessness of a high degree—in essence, *intellectual appropriation* of the French viral isolate."

That wasn't the only dissenting opinion Bivens' group considered. On 21 May and again on 8 June, Bivens says, his full ORI team visited the offices of Dingell's subcommittee. The members of Dingell's staff who met them were accompanied by Suzanne Hadley, once head of the OSI investigation of Gallo, who resigned from OSI before its report was completed and subsequently accused Healy of interfering in the investigation. (Hadley has since been reassigned by NIH to Dingell's subcommittee at Dingell's request.) Bivens says that neither Hadley nor Dingell staffers suggested changing the conclusions of the OSI report. The Dingell staffers did, however, let Bivens and his colleagues read a critique of the report that the subcommittee staff had prepared. A theme of that critique is that charges against Gallo in OSI's first draft report (written by Hadley) were "watered down" in the final version. The softened criticism of Gallo for the disputed LAV sentence is singled out as "perhaps the most egregious instance of 'watering down'"

GALLO VERSUS ORI ON "THE LAV QUESTION"

The disputed clause: The apparent differences between HTLV-III and LAV might be due to the fact that LAV "has not yet been transmitted to a permanently growing cell line for true isolation and therefore has been difficult to obtain in quantity."

ORI Interpretation: Gallo is guilty of scientific misconduct because the clause is intended to mislead the research community with respect to whether LAV had, in fact, been grown in a permanent cell line.

ORI's Supporting Evidence:

1. On its face, the statement indicates that no one has successfully infected a permanent cell line with LAV.
2. The paragraph cites non-French references.
3. Popovic told OSI he believed the paper should have stated that he had successfully infected a permanent cell line with LAV.
4. The original draft of the paper that Popovic wrote included a description of his putting LAV in a permanent cell line, which Gallo deleted.
5. Drafts of the paper did not refer to the French accomplishments with LAV.

Gallo Defense: The highlighted clause refers to the accomplishments of the Pasteur Institute researchers as reported in the scientific literature.

Gallo's Rebuttal:

1. Read in the context of the paragraph, the clause is explaining that differences between American and French findings regarding a new retrovirus that causes AIDS may be due to the fact that the French have not yet been able to characterize LAV.
2. The non-French references are cited only as information about the American virus.
3. Gallo wanted the paper to focus on his lab's isolates.
4. When Gallo first deleted Popovic's reference to growing LAV in permanent culture, Gallo, in his own hand, added the information at the end of the paper. This remained in the paper until the eighth and final draft, and was only taken out at the galley proof stage because two of the scientists in Gallo's lab suggested that the LAV reference at the end of the paper raised more questions than it answered.
5. Gallo had no obligation to write about isolates other than those from his own laboratory.

and 'whitewashing' in the OSI final report."

After assimilating the Dingell subcommittee's critique—which argues repeatedly that the possibility of theft should not be ruled out yet—Bivens' group puzzled over the record on their own. Their conclusion that the sentence about LAV did constitute misconduct "wasn't a finding that just leaped out at us," says Bivens. "It took a lot of work looking at a pattern of behavior."

Specifically, the Bivens team concluded that even if the disputed sentence about LAV can be "technically interpreted to refer to the accomplishments of French researchers, an interpretation that ORI disputes, ORI believes that Dr. Gallo is guilty of misconduct because the statement is intended to mislead the research community." ORI further asserts that Gallo had "a strong moral obligation to facilitate scientific progress" by revealing that LAV had been grown in continuous culture in his lab. His failure to do so, says the report, "impeded potential AIDS research progress with LAV" and "virtually ensured that most researchers would use HTLV-IIIB in AIDS research."

In interviews with OSI, Gallo offered several reasons for not describing his lab's work in putting LAV into a permanent cell line. He said he didn't believe he had the right to publish information about LAV without permission from the French researchers. What is more, if he had done so, he told OSI, it would have appeared he was trying to embarrass the French, who had not had similar success. Gallo also maintained that if he wrote about LAV he would have had to include the French as co-authors in the publication. Finally, Gallo told OSI that his lab had only grown LAV "transiently."

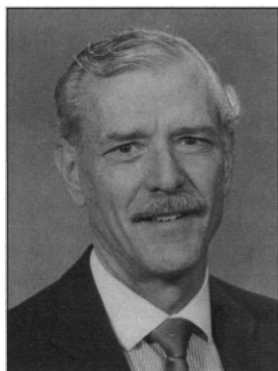
ORI considered each of these arguments and rejected them. Gallo provided contradictory testimony to OSI about whether he could publish on LAV, Bivens' team noted, at some times saying he could. As far as embarrassing the French, ORI noted that Gallo had, in fact, showed little compunction about embarrassing the French researchers in public and denigrating their technique. ORI also found little evidence that Gallo actually believed he would have had to include the French as co-authors if he mentioned the work with LAV by his group. Moreover, ORI cites evidence that Gallo knew LAV had been grown in a permanent cell line in his lab. They also offer various instances in which he denied, in the press and in private, that LAV had been grown in continuous culture in his lab; this formed part of the pattern that led ORI to conclude, "Gallo intended the statement [in the paper] to deceive others regarding the growth of LAV."

Gallo and his attorney, Joseph Onek, were

informed of the potential misconduct finding by ORI in September. "It was quite a shock," recalls Onek, adding, "but I thought it was nonsensical." Onek responded to ORI on 9 November, stating that the "disputed clause is at most ambiguous; it is not false." On 25 November, the ORI team met with Gallo and Onek, at Onek's request. "It was perfectly pleasant," says Onek. "But they ignored all our points."

In spite of such protestations, even some of Gallo's allies aren't buying the line that he did nothing wrong. Nobel Prize-winning retrovirologist Howard Temin of the University of Wisconsin concedes Gallo was wrong not to describe his lab's use of LAV. "That's clearly improper," says Temin. He also calls Gallo's reasons for not describing that work in his paper "obviously silly" and says ORI was "quite right to reject them."

Still, says Temin, the ORI report comes to a "very unfortunate" conclusion because Gallo's behavior, though not collegial, was not misconduct. Temin says he believes misconduct applies to researchers who have falsified "a major thing." In the Gallo case, the misrepresentations were "minor things" says Temin—things that did not affect the paper's conclusions. Temin argues that Gallo's transgressions were a matter of denying credit to a competitor—not serious falsification. Temin



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—Lyle Bivens

also strongly objects to ORI's conclusion that Gallo's failure to describe having cultured LAV impeded other researchers. "LAV and IIIB are the same," he says. Whether researchers got their samples "from Gallo or Montagnier couldn't have made any difference in the world."

Although the ORI report might well be construed as a slight to NIH Director Healy, who approved the OSI version clearing Gallo, Healy says she doesn't see it that way. She claims there is much room in the Gallo matter for legitimate disagreement. "I know how much we struggled with all of the facts. It was definitely clear that there was a large element of judgment." But, adds Healy, without new data "I'm not reversing what I thought."

Others who were involved in the OSI process are angrier at having their judgment rejected. Former OSI director Jules Hallum,

an investigator on the Gallo case, says, "The ORI report is filled with statements about what Gallo intended. How did they get into his mind?" Hallum says he believes the ORI team was swayed by the Dingell group's critique. "I think [Bivens] bought their argument," he says. And even if Bivens didn't simply accept the arguments in the Dingell staff document, Hallum brands the visit "a great danger to the American scientific integrity enterprise" because "it's going to make ORI look like a subgroup of the subcommittee."

When Bivens was told of Hallum's opinion, he said he doesn't see why it's improper for the ORI team to visit Dingell's staff. "If it's improper for us to go to the subcommittee to review their critique, is it improper for us to have gotten the Richards committee critique? I see it as the same sort of thing—getting input from knowledgeable sources." In addition, Bivens denies that his team "bought" the argument laid out in the Dingell document. "If we bought their argument," he said, "we would have come out with a stronger finding about misappropriation."

Indeed, from Hadley's point of view, that's just the weakness of the ORI verdict: It doesn't get to the bottom of the possible misappropriation. Hadley applauds the misconduct finding, which she says is "fully supported by the evidence." Yet she says the ORI report "stops short of the truth." Specifically, Hadley believes ORI shirked the job of settling the misappropriation question once and for all. "It says to me again that HHS is just not able to deal with that issue," she says. She finds it "astonishing," she says, that ORI decided Gallo had intended to deceive others with the LAV statement yet didn't link that finding of misrepresentation to the question of misappropriation.

The only people who express satisfaction at the verdict are members of the Richards panel. "We're pleased to see that our report appeared to have had some influence on ORI," Richards told *Science*. Alfred Gilman, a chair of the pharmacology department at the University of Texas Health Sciences Center and a Gallo critic who was a Richards panel member, says the ORI findings bring the investigation's conclusions "back into register with what we thought." The OSI report, Gilman says, missed "an overall pattern" that "worked out for the greater glorification of Gallo."

Whatever the general satisfaction level, don't bet on this verdict ending the Gallo affair. Though Popovic has yet to decide whether he will appeal, Gallo has already said he will. The appeal will be heard in a public forum and is likely to take place before summer.

—Jon Cohen