# II: The Untold Story of HUT78

*When Robert Gallo announced he had isolated and grown the AIDS virus, he didn't mention those who established the key cell line. A 1988 NIH inquiry quietly resolved the credit issue. But the NIH director has decided to revisit the matter and look into the distribution of income from the AIDS blood test. Here, in the voices of the participants, is what happened*

**"Maybe I'm a little naive in some things, but I really don't understand what I'm supposed to have done.**

**"I know what credit I gave to the other side, even though I knew what they had and what I had and [that] we had more at that time. I know science comes in steps; I know I stand on the shoulders of a lot of people and jump from there. And I know that they stand on mine and then I stand on theirs.**

**"To me, it's just a jigsaw puzzle, and we keep playing with it until we get vistas out of little corner pieces. We are all involved in this catalytic game of using each other, and that's the nature of science.**

**"I'm wrong in what I do scientifically more [often] than most people because we tend to do more, we tend to speculate more, and we try to ask larger and long-term questions more. Just as Lord Rutherford was garrulous, loud, and provocative, and J. J. Thompson was extremely quiet, withdrawn, and introverted, we all vary.**

**"I really don't quite understand what the hell it is [that] I'm supposed to have done."**

Robert Gallo has run a laboratory under siege for much of the last decade. For several years he had to weather the accusations of Luc Montagnier and the Pasteur Institute who argued that he tried to hog the credit for the discovery of the AIDS virus—and to grab 100% of the lucrative patent on the blood test made possible by that discovery. Once that dispute seemed settled, he found himself under the microscope of *Chicago Tribune* journalist John Crewdson who has for more than 3 years acted as if he, Crewdson, were the relentless virologist while Bob Gallo was a heretofore undiscovered human retroscientist. And now it's Gallo's peers—a pair of blue-ribbon panels—probing his scientific probity.

Perhaps the current round of investigations (see previous article) will yield nothing new. But in the search for smoking guns or definitive exonerations, Gallo's investigators often overlook both the everyday ethical quandaries the Gallo team has faced and their responses to them: When and how should others be credited for their contributions, and when is it acceptable to withhold credit? When should errors or omissions be corrected in the literature, and just how prominently should this be done? When is it acceptable to control the distribution of cell lines, clones, and the like, and when should these be deposited in public access repositories?

This account—an in-depth investigation of two different eras of Gallo lab history based on scores of interviews over several months' time—analyzes just these sorts of "hard choices" made by the Gallo team. Sometimes the choices resulted in *both* grand achievement and residual feelings of fellowship and pride among the scientists involved. This was largely true with the discovery in 1979 by Gallo researchers Bernard Poiesz and Frank Ruscetti of the first human cancer retrovirus, HTLV-I. The Gallo group found the virus in a cell line that had been established in a separate lab, John Minna's Clinical Oncology Branch, then of the Veterans Administration, by researchers Adi Gazdar and Paul Bunn. All three—Minna, Gazdar, and Bunn—were listed as coauthors on Gallo's paper on HTLV-1.

In contrast, only a handful of years later, the Gallo lab's choices were very different, and a major scientific accomplishment became tainted by conjecture, innuendo, and a sour taste left in the mouths of scientists who had once collaborated closely with the Gallo team. On 4 May 1984 the Gallo team announced, in a landmark *Science* paper, "Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS." The group had not only managed to isolate the mysterious AIDS virus: Gallo retrovirologist Mikulas Popovic had grown it in large quantities for the first time, in cells he dubbed H9 that were not killed by the virus. But authors Popovic and Gallo *et al.* did not mention the origin of H9. Years later, that cell line was shown to have been cloned from a line established by Gazdar and Bunn in the Minna lab; they had named it HUT78 and had freely donated it to Gallo, just as they had the cell line that contained HTLV-I. But, in Gallo's lab, HUT78 underwent a name change that deprived Minna's researchers of any credit for the Gallo success—and perhaps also of a share in the royalties that would come from the AIDS test.

That something like this might have happened was a source of conjecture at scientific meetings around the world for years after the Gallo paper was first published. By 1988, in the course of his crusade to expose the underbelly of the Gallo lab, journalist Crewdson had begun asking questions about the cell line, thereby triggering a little noticed investigation carried out by the National Institutes of Health on the explicit orders of outgoing National Cancer Institute chief Vincent DeVita and then NIH director James Wyngaarden. The result was a three-page "Letter to the Editor" published in 1989 in a small circulation journal (*AIDS Research and Human Retroviruses*) that finally set the record straight.

But the NIH probe never seriously examined why Gallo and Popovic hadn't mentioned the Minna group or their cell line in the original paper. Nor did it look for lessons to be learned from the episode. Nor even did it look at whether Gazdar and Bunn, in retrospect, deserved anything more than the appearance of their names (Gazdar's as cosignatory; Bunn's in a reference) in that letter to the editor published in a journal of limited circulation.

Now all that has changed. Acting NIH director William Raub

## Selected Dates in the Gallo Saga

**10 September 1976:** Doris Morgan and Frank Ruscetti in Robert Gallo's lab characterize in *Science* interleukin-2, naming it T cell growth factor.

**13 December 1977:** In John Minna's lab, Paul Bunn brings Adi Gazdar T cell tumor sample HUT78 from patient suffering from mycosis fungoides; Gazdar cultures them.

**18 May 1978:** Bunn brings Gazdar T cell tumor sample HUT102.

**1 February 1979:** Gazdar hands two cell lines—HUT78 and HUT102—over to Ruscetti and Gallo fellow Bernard Poiesz.

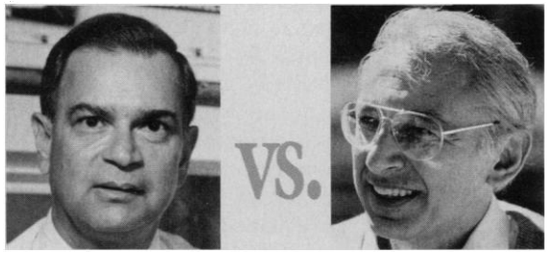
**2 January 1980:** Mikulas Popovic arrives in Gallo's lab.

**March 1980:** Gazdar, Carney, Bunn *et al.* publish paper in *Blood*, reporting the establishment of permanent T cell lines HUT102 and HUT78.

told *Science*: "The issues of HUT78 are within the scope of [the current investigation]." He added: "We'll pursue them to the detail necessary—cell cultures, motivations, and the like." In fact, Raub hasn't waited for the committee reports to look at whether Gazdar deserved more than just public acknowledgement: he immediately asked NIH's patent counsel whether Gazdar's contribution "established the basis for coinventorship [of the patented AIDS blood test]." That patent has reportedly yielded Gallo and Popovic (who recently left NIH to head the Virology and Immunology Department of New Mexico State University's Primate Research Institute) approximately $100,000 a year for the past 3 years. Gazdar has gotten nothing above his normal salary, and now Raub says: "NIH will take the appropriate steps to assure that Dr. Gazdar has, at our hands, not only the full credit for what was an important contribution, but also his rightful participation under whichever of the two income streams [patent royalties and NIH awards] makes sense. I am intent on doing right by him."

This is, of course, welcome news to Gazdar who hadn't raised a formal complaint until quite recently. For years, he had wondered whether H9 might not have come from his cell line, but a lawyer friend in the government had suggested that any public doubts he might raise could upset the delicate negotiations going on between the French and U.S. governments over the Montagnier-Gallo patent issue. In fact, it was only after journalist Crewdson showed him photocopies of the Popovic notebooks, which made it clear to Gazdar that Popovic had been using HUT78, that Gazdar fully realized how hurt he felt: "It's not only money," he told *Science*, "it's attribution. Here's a line that is used worldwide for AIDS testing and no one knows that it came from my laboratory."

But Gallo told *Science* that Gazdar's plea for credit is a "pathetic joke." Says Gallo: "I don't consider it so brilliant. In my mind, there is no credit for a cell line. If it happens by accident that you have a cell line, so freaking what? We didn't patent the cell line; we patented the process. We don't take any claim or credit for even cloning the damn thing. Mika [Popovic] spent months cloning it. Look at his records: there's a lot of work there—far more than Gazdar's."

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One former Gallo fellow—HTLV-I codiscoverer Poiesz, who today heads up the hematology-oncology departments at the State University of New York's Syracuse Medical Center—sees it differently: "I think Adi [Gazdar] would appropriately be miffed if someone had his cell line [and] called it a different name."

Gazdar himself puts it a bit more personally. To Gallo's claim that it doesn't matter who invents a cell line, Gazdar says: "Well, then the next question is: Does it matter who discovered the virus? That does matter, doesn't it?" And to Gallo's claim that it's luck that usually leads to the discovery of a cell line, Gazdar laughs: "I'd say the same [about discovering a virus]."

This, then, lies at the heart of the "HUT78/H9 affair": What constitutes a scientific achievement deserving of credit? Were reasonable efforts made to establish H9's paternity? And most important, what lessons are to be learned from the way this small group of outstanding scientists did their science . . . and from the way they treated their scientific colleagues?

### I. The Collaborative Era

To John Minna, NCI–Navy Clinical Oncology Branch chief and Adi Gazdar's boss, the only lessons worth learning are those embedded in the discovery of HTLV-I—an achievement he pleaded with *Science* to emphasize even if it meant downplaying the vindication of his team for its lost credit in the discovery of the cell line that first grew the AIDS virus. And indeed, the sequence of events that culminated in the HTLV-I coup reflects values scientists hold most dearly: commitment in the face of near universal skepticism, perseverance, flashes of brilliance . . . and especially cooperation and generosity of spirit. But in these regards, HTLV-I's success highlights much that was absent in the HUT78/H9 affair.

The seminal event that drove John Minna's lab and Bob Gallo's lab together for a fruitful couple of years of collaborative science occurred on 1 February 1979. Adi Gazdar—then a 41-year-old pathologist who had been born in Bombay and had picked up an M.D. degree from London University—handed two cell lines, HUT78 and HUT102, over to Gallo investigator Frank Ruscetti. This donation to the Gallo lab was the consequence of a carefully crafted deal: Ruscetti, who had been a key figure in the discovery of the human T cell growth factor interleukin-2, had agreed to provide IL-2 to Minna's group to help them grow cell lines; in return, Gazdar would pass promising cell lines to Gallo's group who were hunting for retroviruses and were particularly interested in lymphomas from leukemic patients.

Ruscetti won't speak of what happened next. It is one of the many sadnesses that dog Gallo lab successes that Ruscetti now feels compelled to tell not only journalists but close colleagues that he cannot take the emotional stress of discussing any of the events of those days. Says one Gallo associate from those days: "Personal enmity developed between Bob and Frank."

Fortunately for historians of science, Ruscetti co-worker Bernie Poiesz remembers subsequent events well. Poiesz had joined the Gallo lab as a fellow shortly after Gallo had experienced a debacle: In

**July 1980:** Poiesz leaves Gallo lab for SUNY, Syracuse, leaving passages of HUT78 (labeled HUT78L) in Gallo's freezer.

**December 1980:** Poiesz, Ruscetti, Gazdar, Bunn, Minna, and Gallo report in *PNAS* the isolation of the first human retrovirus, HTLV-I, from HUT102.

**June 1981:** First cases of what will eventually be called AIDS are discovered by UCLA researcher Michael Gottlieb.

**August 1981:** Dean Mann, working in the Laboratory of Human Carcinogenesis on interferon production by HTLV-I infected cell lines, HLA-types three differently labeled passages of HUT78 in the Gallo freezer. He finds they have different phenotypes.

**18 March 1982:** Gazdar deposits HUT78 and HUT102 in the American Type Culture Collection.

**14 June 1982:** Gazdar sends Poiesz—now at SUNY, Syracuse—passages of HUT78.

1975, Gallo announced the discovery of the first human retrovirus, HL23, to great acclaim, but several months later he was forced to admit that HL23 was nothing more than a simian virus that had contaminated his cultures. Recalls Poiesz: "The HL23 episode left a lot of people wary about making new claims about human retroviruses. Frank and I were fresh faces on the scene."

Showing uncommon courage considering that many top researchers had fled the field after a decade of failures, Poiesz and Ruscetti proposed to hunt for retroviruses and "Bob gave his imprimatur." One key to what was to happen later was that, just a few months before joining Gallo, Poiesz had performed a clinical rotation under Adi Gazdar and another Minna lab scientist, clinical oncologist Paul Bunn. Bunn had recently joined Minna, bringing to the lab an interest in lymphomas. Acting as the clinician who set up protocols and obtained materials, Bunn handed Gazdar what were to become two of the most famous cell lines ever established—HUT78 and HUT102—and Gazdar cultured them.

Shortly thereafter, as Poiesz recalls, "Adi, whom I had befriended, called and asked if he could be of help. What I suggested was that he and Paul could get me access to more of their patients. He told me he had two cell lines from those patients. One was HUT102 from a patient I had actually helped take care of when I was on the clinical side. And he had another, HUT78. So we agreed that he would send us those two cell lines, and we would include [Gazdar and Bunn] in the analysis being pursued." Moreover, Poiesz promised Gazdar "that we would include him as a coauthor on anything we found from those cell lines. And that's what we did."

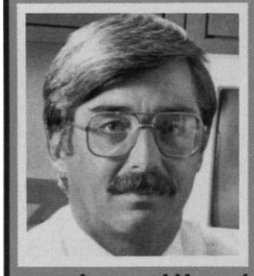
But did they? The Gallo team found no virus in HUT78 but HUT102 was another matter: There they discovered what they were to name human T cell lymphoma (later, lymphotropic) virus, or HTLV-I, the first human retrovirus ever discovered that could cause cancer. As promised, Gazdar appeared as a coauthor on the Gallo paper announcing the discovery of HTLV-I. Even these many years later, Gazdar's branch chief John Minna waxes proudly: "I think [the collaboration] was the perfect example of how synergy could happen as part of the NIH intramural program. [As clinicians] we were trying to do something about lung cancer. But it turned out our work in trying to grow human tumor cells was synergistic with the work [of] growing human T cell lymphoma cells and it happened that those things came together."

Still, it wasn't all sweetness and light. A Japanese researcher at Kyoto University, virologist Yorio Hinuma, would soon trigger a bitter public squabble with the Gallo lab over credit for linking HTLV-I to leukemia. (The U.S. group had thought HUT102 came from a patient with mycosis fungoides but the Japanese recognized the syndrome to be a form of leukemia, eventually forcing Gallo to redefine the L in HTLV as leukemia rather than lymphoma.) But even in the months leading up to the HTLV-I discovery, there were moments filled with rancor.

Poiesz today is reluctant to discuss publicly just how difficult it sometimes was for him to broker the collaboration between his former clinical mentors—Minna, Bunn, and Gazdar—and his then research Svengali, Gallo. But one former Gallo associate, who left on the best of terms with the mercurial retrovirologist, remembers a telling exchange he had with Poiesz. Specifying that he not be identified because "this is an area where substantial retribution has been exercised in the past, and I have no reason to put myself at risk," this scientist recalls: "Bernie, who has never been short for words, once said: 'You know, one time I had Gallo and Minna both in a room and all I wanted to do was punch out both of them.' Here's a young guy [arbitrating] between two giants who were fighting about typical scientific ownership and jealousy issues."

Poiesz concedes that "there was tension between [Minna and Gallo] . . . and a little bit of rivalry." And Bunn reluctantly acknowledges that "it's fair to say Minna and Gallo weren't best friends—these are big scientists with big egos." Which is why Bunn sees "the whole story [as] a great tribute to collaborative science. Here are people doing clinical studies and [when] specimens get into the laboratory, the first human cancer virus is found, a way to detect that virus is found, IL-2 is found, a way to clone the gene for IL-2 is found, and out of that HIV came too."

How different things became after Poiesz, the conciliator, left.



### Poiesz on Gallo:

*The Pluses:*

*"I'm forever grateful to [Bob] for my time there—probably two of the most exciting years of my life. He created the setting where a person such as myself—an M.D. who was a clinical postdoc—could learn from so many expert people how to conduct science in a technically competent way.*

*"He does an excellent job of organizing such a large group of people with diverse personalities, backgrounds, and scientific interests into a cohesive team, and he's able to maintain the energy of the lab via his own personal energy."*

*The Minuses:*

*"If you consider the Laboratory of Tumor Cell Biology a basketball team, there's a general manager of the team, a coach, and players. The general manager takes credit for putting the team together, keeping it logistically on the road, and balanced at various positions. The coach teaches and deploys certain people for certain tasks. And the players take the shots. In [our lab], I was the forward taking the shot, Frank Ruscetti was the coach, and Bob Gallo was the general manager. I should wind up getting the credit for taking the shots and making it. Sometimes perhaps the general manager may have been wanting to get credit for making the shot."*

### II. The Isolationist Era

Minna remembers well the schism that developed between his lab and Gallo's: "Adi [Gazdar] and I had published several papers on retroviruses and [their regulators] in humans. We had every legiti-

**16 September 1982:** Bunn asks Gazdar's technician, at Gallo's request, to send over fresh passages of HUT78. This will be called HUT78B.

**20 May 1983:** Gallo and Montagnier publish papers in *Science* claiming to have isolated AIDS-related viruses from different patients. Montagnier's LAV will prove to be what is today called HIV. Gallo's is HTLV-I.

**October 1983:** Mann again HLA-types Gallo HUT78's, this time including the fourth passage designated HUT78B for Bunn. The latter's phenotype also suggests mixed-up cell lines. Separately, Mann advises Popovic, now hunting for a cell line in which to grow the AIDS virus, to look for a CD4+ cell line.

**24 October 1983:** Gallo researchers infect HUT78 with Montagnier's LAV.

**5 December 1983:** By this date, Popovic was using the designation HT for the cell lines he had developed from HUT78.

**30 March 1984:** Gallo submits four papers to

mate right and expertise to [get back into retroviruses]. But Dr. Gallo made it very clear that if our branch would start investigating retroviruses, he was going to consider this big league competition."

How precisely did Gallo's attitude display itself in practice? Minna recalls that "Bob Gallo had people come down to my lab to learn how to make monoclonal antibodies. (Because of our hybrid cell work, I was one of the first groups on campus making monoclonal antibodies with hybridomas.) But all of a sudden I discovered that they were down there and didn't want to talk to me about what they were doing. Now, I am a big boy and it became very clear that they weren't interested [in working with us], so I said, 'Fine, why don't you go ahead and learn what you need to and you can go back!' "

They did, and that's when problems that would later come back to haunt Gallo's lab first appeared. By the latter half of 1982, Gallo had become aware of the mysterious disease that was to be called AIDS. At the time, no one knew for sure what caused the disease, although many researchers thought it was likely to be a virus, and Gallo in particular thought it could be a retrovirus. He even thought it might be HTLV-I or an HTLV-I relative, because AIDS wiped out the same kind of cell, the T cell, that HTLV-I infects.

Gallo placed his bets on a relative newcomer to NIH to grow the still hypothetical AIDS virus. Poiesz was long gone; Ruscetti had become disaffected. Now Mikulas Popovic, a Czech retrovirologist who had a doctorate from the Cancer Research Institute of the Slovak Academy of Sciences in Bratislava, Czechoslovakia, began to search for a cell line that would show susceptibility to the virus.

Today, Popovic tells a sketchy tale of the period, perhaps because his English remains shaky or perhaps because he feels on the defensive. But based on hours of interviews with others as well as with Popovic, and based on the review of numerous documents, this much is known.

Bernie Poiesz had left samples of HUT78 in the Gallo freezer when he moved on to Syracuse in July 1980—freezes that were to be designated HUT78L (for Litton Bionetics, an NIH subcontractor on whose premises Poiesz briefly worked). By 1981, there were at least two other freezes designated HUT78 in the Gallo lab. All three found their way into the hands of Dean Mann. Mann now heads the Section of Immunogenetics in NIH's Laboratory of Viral Carcinogenesis, but, in 1981, Mann was working in the Laboratory of Human Carcinogenesis and was interested in interferon production by HTLV-I–infected cell lines. In the course of his research, Mann HLA-typed the three samples designated HUT78 in the Gallo freezer. HLA typing is a way of immunologically characterizing cells, and, when Mann did this to the samples in the Gallo freezer, he found that they were "different in their HLA phenotypes. A technician told me that she thought they were mixed up," he recalls. To Mann, it appeared that more than one person's cells might have gotten into two of the three samples.

A year later, Mann again HLA-typed the three sets of HUT78 samples as part of his interferon studies, this time also typing a fourth sample designated HUT78B [the B for Paul Bunn, who had ordered a Gazdar technician to send a passage to the Gallo lab at Gallo's request]. Says Mann, "Some of the passages had B cell markers on them—obviously B cell lines, not T cell lines." Since Mann was interested only in the cells' interferon production, "The real HUT78 was, as far as we were concerned, irrelevant."

But in 1983, questions about the real HUT78 became very important to Mika Popovic. The Czech was by then assigned to find a cell line in which the AIDS virus would grow. Learning this, Mann advised Popovic to look for a "CD4+ cell line that has MHC (major histocompatibility complex) class 2 [markers] on it." Mann's point was that, in AIDS patients, T cells with this characteristic disappeared, suggesting they were the main targets of the AIDS virus. This made them seem promising even though no one at the time could have imagined that such cell lines would not only "engage" the virus but would resist its killing power, allowing the virus to grow and be studied. Since HUT78 was a human T cell line with the desired characteristics, Popovic was eager to try it; but then came the question: Which of the samples in the Gallo lab freezer—each marked HUT78 but each typed by Mann and found to be different—was the HUT78 he should work with? He decided to choose one sample—he didn't tell *Science* which—and clone individual cells from it so that he would have pure populations of cells, each derived from a single parent cell.

Why the cloning? In Uppsala, Sweden, doing postdoctoral work in 1974, Popovic had identified "the most common retroviral contamination which occurs in the laboratory—squirrel monkey virus." From this experience, as he puts it today, "obviously I got a fear" that the HUT78s, one or all of them, might be contaminated—particularly by HTLV-I. Retroviruses, he knew, have the capacity to infect a wide variety of cells, but not kill them; instead, retroviruses can "hide" in cells for a long time and then suddenly start to reproduce. So Popovic's solution was to clone cells from one or more of the samples labeled HUT78 . . . and to clone again and again to get a "clean" cell line.

To Bob Gallo and some of his researchers, Popovic was a master at cloning. Says one former Gallo associate: "Popovic made a major, major contribution by deriving a clone that was resistant to HIV's [killing power]. He grew up in Czechoslovakia where all of this old stuff with virus strains and susceptibility and cross-resistances with all the different chicken viruses was developed. So he proceeded with the experiments, knowing stuff that by now is almost forgotten. Sitting in a corner of this little convoluted room where he worked, puffing on his pipe, putting it down on the hood, pipetting, picking up his pipe again, working in a very secluded, studious way, [Popovic tried] a lot of stuff that is really almost antiquated techniques, almost alchemy."

But Popovic's achievement wasn't magic. He grew what was then called HTLV-III—the Gallo team's early name for HIV—and he grew it in several clones, most particularly one dubbed H9. And that's what Popovic and Gallo wrote in their electrifying 1984 paper in *Science*: "We have used clones H4 and H9 for the long-term propagation of HTLV-III from patients with AIDS and pre-AIDS." Where did the clones H9 and H4 come from? The paper addressed this question as follows: "Several neoplastic human cell lines established in vitro were assayed for susceptibility to infection with . . . many of the more cytopathic retroviruses isolated from AIDS patients. One neoplastic aneupoid T cell line, derived from an adult with lymphoid leukemia, was found to be susceptible to infection. . . . This cell line, termed HT, has produced HTLV variants in

*Science* reporting the detection and isolation of the AIDS virus, which he now calls HTLV-III.

**23 April 1984:** U.S. government lawyers apply for patent on the Gallo AIDS test.

**4 May 1984:** Popovic and Gallo announce, in the first of the four *Science* papers submitted on 30 March 1984, that they have "used clones H4 and H9 for the long-term propagation of HTLV-III from patients with AIDS and pre-AIDS."

**31 May 1984:** Jay Levy of the University of California at San Francisco submits to *Science* a paper reporting the isolation of his AIDS virus, which he has grown in HUT78. He claims to have actually isolated the virus in early November 1983, which he believes precedes Gallo's isolation of the virus.

**July 1984:** Mann HLA-types five samples labeled HUT78, this time including a fresh passage Popovic says he got from Bunn. Bunn does not recall this and no record exists of it in the Minna lab.

sufficient quantities to permit the development of specific immunologic reagents. . . . "

Where precisely did HT come from? The paper made it clear that this was a line from which a whole series of clones had been made, of which the two best were H4 and H9. But whose patient was this supposed leukemic sufferer? The reader might well have assumed HT was a brand new cell line discovered by the Gallo team in an unnamed patient. Both Gallo and Popovic today point out that the paper purposely never said anything of the kind. But even if the reader of that paper had been as knowledgeable as Adi Gazdar and Paul Bunn were at the time, he'd have been unable to identify the patient from the Gallo team's description. The two clinician researchers, who had worked with that very patient, would have said the patient suffered from Sézary syndrome, a form of mycosis fungoides, not that he was leukemic.

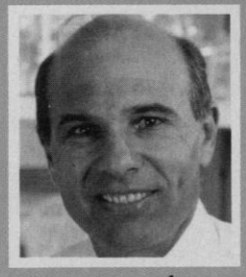
And then, of course, neither HUT78 nor Adi Gazdar's name nor Paul Bunn's was mentioned anywhere in the text of the paper, not even in the references.

Why not, when the Poiesz deal had specified that the Minna group would be included in any papers based on work done with their cell lines? Mika Popovic says he didn't know at the time what HUT78 was. Yes, he admits, he was working with HUT78. Yes, he was suspicious that HT, the cell line from which the H9 clone was derived, was HUT78 and, yes, Bob Gallo and Popovic both claim that they consistently told anyone who asked them at scientific meetings that they thought HT *was* HUT78. But, they insist, they couldn't be sure enough to include that information in their paper. Why? Because Dean Mann's HLA typing showed that it was impossible to tell what the real HUT78 was, they say.

But not everyone accepts this explanation.

### III. What's in a Name?

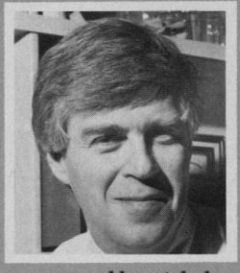
Bernie Poiesz, friend of Gazdar, Bunn, and Minna, but long-time associate of Gallo, says: "People thought H9 was HUT78 from the very beginning. Most people suspected that H9 could be just a clone of HUT78 that was somehow selected for better propagation of HIV—it didn't die as much as the parent cell line and yet could still produce virus." Another Gallo ex-investigator goes even one step further. Requesting that he not be named, he told *Science*: "It was known to everyone—*and* Mika Popovic—that H9 was a derivative of HUT78. Mika told me [this]. He shrugged and said something like, 'Of course, it was a derivative.' "



**Minna on Gallo:**

*"Bob Gallo is a very charismatic individual and they'll be writing plays about this guy 50 years from now. [He] has both participated in great scientific activities and shot himself in the foot. He could be utterly charming one moment and not so charming the next."*

**O'Brien on Gallo:**



*"I have been involved with fraud many times because one of the things that we do is straighten out confusions in genetic terms in cell lines. And I know when I run into someone who is crooked and Bob Gallo is not that person. He might be arrogant and he might be abrasive and he might even be careless occasionally. But he's not fraudulent."*

But just when that conversation took place isn't clear, though what is clear is that, today, Gallo and Popovic have strong feelings on the matter. As Gallo tells it, it was enough that his retrovirologist had considered two HLA typings before the *Science* paper came out in the spring of 1984 and yet another in the fall of 1984. The result of all three, says Gallo, was the same: no prospect with currently available technologies to remove the confusion about the characteristics of the "real" HUT78. "I didn't want to spend the rest of my life wondering about the origin of HT," he told *Science*, adding, "We clearly never claimed we developed the line in the paper." And then Gallo went one step further: "We made it clear to anyone who asked or whomever we talked to" he said, "that it probably is HUT78 but we have trouble proving it, period."

Other scientists remember things differently when no Minna team members were in Gallo's audience. Bernie Poiesz told *Science*: "The thing back then, to be frank, was that it was being implied that Mika started from scratch and made this cell line. This was implied at least in the talks that I heard."

Popovic strongly contests this. But, unlike Gallo, he says that when scientists met him at scientific meetings and asked him whether H9 wasn't HUT78, "I became irritable." In his Czech-inflected English, he adds, "It took me a lot of time to figure out how is it possible they had so mixed the HLA types. They should know that they did some mixture for cultivation. Why they didn't tell me this when they give me HUT78?"

Popovic does not make clear who the "they" is. If he meant his former colleagues Poiesz and Ruscetti who had handled the cell lines before Popovic ever came to NIH and had left them in the freezer, he certainly never discussed the matter with them, even though he talked to them over the years. And if he meant Gazdar and Bunn, they would ask what evidence he had that they had ever mixed up a HUT78 line—and they too never knew the extent of Popovic's problem. Popovic says flatly that he had never heard of Gazdar at that time—even though Gazdar was the lead author on the paper describing the original isolation of HUT78, a paper Popovic seems not to have gone back to read despite his years of travail figuring out what HUT78 really was. When, in 1984, Popovic finally contacted Paul Bunn at Gallo's suggestion, he still didn't explain his quandary . . . or, indicates Bunn, he would have helped him solve it.

So there are two core questions that can be asked about the Gallo lab's failure to definitively establish the parentage of H9. One relates to the period prior to the spring of 1984: Why, *before* publishing

**24 August 1984:** *Science* publishes Jay Levy's paper.

**5-6 September 1984:** At Popovic's request, Bunn uses flow cytometry to test H9, H3, and an early passage of HUT78 Popovic has provided. His conclusion: "They looked pretty much the same."

**22/29 December 1984:** Popovic and Gallo publish in *The Lancet* a paper comparing all the cell lines in which they'd grown HIV. HUT78 is mentioned but not related to their HT or H9.

**Early 1985:** At a ski meeting Poiesz asks Mann about rumors concerning H9's provenance. Mann says his HLA typing suggests that the cell line labeled HUT78L had the same HLA type as H9. Poiesz recognizes HUT78L as the line he left behind and tells Mann. Mann says he later told Popovic this.

**1 February 1985:** Levy *et al.* show in *Science* that his isolate is genetically similar to Montagnier's.

**7 February 1985:** Muesing *et al.* in *Nature* show the

such an important paper, didn't Popovic try harder to sort out the provenance of his mysterious H9? Popovic's answer is straightforward: "The papers to *Science* were written out very quickly under the pressures [that] we could not hold back because [they expected] the blood bank assay [to] work. So I told what we knew at that point about the cells. I wrote what is the phenotype of it, which was essential information at that point." Gallo too points out that people were dying and the faster you could get the blood test out, the better. And then he adds a host of other reasons why it should not have been incumbent upon Popovic to explain his confusion.

Not only is the credit for discovering a cell line unimportant in the Gallo playbook and not only had Popovic done far more work than Gazdar in making a useful clone from the line, but "it wasn't one cell line, it was many that we could use, and we happened to use in the paper the HUT78 clone." Says Gallo today, "The number of cell lines the lab succeeded in was not one, it was at least four and I think more like six. And in some respects, Ti7.4, Molt3, and CEM were better than the parental HUT78 we had."

This, though, raises the second core question: Once the paper was published and the blood test patented, and Popovic was knowingly growing HIV in HUT78—why then didn't Gallo and Popovic get to the bottom of the H9 mystery?

### IV. The Gallo Explanation

To Bob Gallo, a paper he and Popovic published in *The Lancet* in December 1984 relieves the two of any further responsibility to Gazdar. He points out that it both mentions HUT78 and references Adi Gazdar. Indeed, that paper lists all the cell lines in which the Gallo team had by then grown the AIDS virus. In fact, it documents their comparative ability to do so, showing H9, for example, to be better at that particular task than HUT78. But the *Lancet* paper still doesn't connect HT and its clones to HUT78. Says Gallo: "The fact is that we had a lot of other things on our mind to do that were important. Maybe I'm insensitive to somebody's feelings about this. It never dawned on me that this was so tremendously important. But I react very strongly against someone saying, 'Oh, well, we would have done this experiment or that,' because that's bull. People would have had to have their heads in caves because everyone knew that we could infect all those other lines."

But one scientist cum troglodyte, Bernie Poiesz, says: "First, I think you should assign the correct nomenclature for the cell line so people understand scientifically what reagent they're using." Then Poiesz makes a different point: "Back then, people were trying to find out the right way to grow HIV. It was clear that the French had propagated it, but their cultures of normal T cells left something to be desired. It was very hard to bulk produce it, and you wanted to be able to bulk produce it. So Mika's finding that you could get this virus into an immortal T cell line, and grow it without [extremely expensive] IL-2, was a very important step. If you wanted to do that in your own laboratory, it was helpful to know what line was best."

But what line *was* best? Before the *Lancet* paper, you couldn't have guessed that the Gallo team believed H9 was superior at growing AIDS—after all, you would have had no way of knowing the team had ever used HUT78. To complicate matters, Jay Levy of the University of California at San Francisco announced in a paper published by *Science* on 24 August 1984 that he had successfully grown HIV in HUT78—the standard cell line, not a clone he had derived from it. (Indeed, Levy has long claimed that he cultured the virus *before* Gallo and Popovic did.) So, a researcher at the time might easily have been confused about the relative efficacy of HUT78 and H9 for growing the AIDS virus.

Once the *Lancet* paper announced that Gallo believed H9 to be markedly better than HUT78, a researcher would have wanted H9. And yet, until about a year ago, he couldn't get it from the American Type Culture Collection (ATCC) because Gallo hadn't deposited anything but the *infected* H9 in the ATCC (and under its patent provisions at that).

Why didn't Gallo place what he was contending to be a superior cell line in the ATCC for all researchers to use? (Minna's group had donated passages of both HUT78 and HUT102 to the ATCC on 18 March 1982 and NIH has long encouraged its researchers to submit major reagents to repositories like the ATCC as soon as possible.) Gallo argues that he simply "didn't think of putting it into the ATCC. I really thought that you sent cell lines to the ATCC when they were original, new cell lines. One thing I was sure of: We didn't originate that line; we originated the clone. Put it another way: If we did originate the line, I could not tell when or where or how." Then he added: "No one asked me to deposit anything to ATCC." But when reminded that the ATCC Cell Culture Department head Robert Hay asked him numerous times, he said, "Oh, you mean the guy from the ATCC. But they want to send out the cell lines for business [purposes]."

Then Gallo makes still a different argument: that his lab shares cell lines with anyone who asks. Yet, he told *Science*: "I prefer to have the right to know who is working with H9 and how they were going to work with it for purposes of HIV isolation at the beginning, period. The answer is that simple. If you've got evidence that we didn't make H9 available to somebody, tell me."

While there is no evidence that H9 was withheld, there is evidence that Gallo has refused requests upon occasion. NIH retrovirologist Mal Martin was denied a reagent in an incident often referred to, even by Gallo, within NIH circles. And one former Gallo lab member, on the promise that *Science* would not identify him, said he had personally witnessed Gallo keeping lines from others.

And finally, some scientists have questioned Gallo and Popovic on philosophical grounds: Were they doing good science? Says John Minna: "When the unexpected pops up, you have to be absolutely rock sure of your data. You have to be very sure of your reagents, materials, the assays you're using to get the results, the people working with you who are generating that data. So . . . if you now work out a condition for isolating a virus, and this is obviously a very important virus, it's absolutely key to know how you did it."

And it is this line of argument that perhaps hurts the Gallo team the most. Many scientists—even some biologists—think that a lab that occasionally experiences cell line contaminations must be a sloppy lab. Every researcher *Science* talked to who has ever dealt with cell lines hotly disputes this. Adi Gazdar himself says: "Cell mix-ups happen in every lab doing large cell cultures. I just recently had a very embarrassing situation where a cell line I thought was derived

genetic sequence of Gallo's HTLV-III to be almost identical to Montagnier's LAV.

**March 1985:** NIH scientists Arnold Rabson and Mal Martin publish an article in *Cell* that finds the degree of similarity between the French and Gallo isolates "surprising in view of their independent isolation."

**28 May 1985:** A patent is granted Gallo for his blood test; no action has been taken on the French application even though it had been filed 4 months before Gallo's.

**6 September 1985:** Popovic pens memo (see figure, p. 1506) to Gallo relating history of his efforts to determine the provenance of H9. He says Gazdar will "shortly" provide an early passage for yet another paternity test. This test occurred only after NIH ordered it 3 years later.

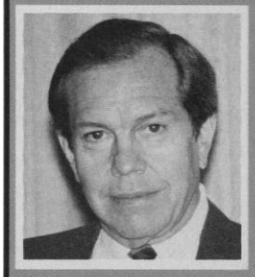
**22 November 1985:** Mal Martin and others conclude in *Science* that American and European AIDS isolates differ as classes...except for the Gallo and LAV isolates, which are similar.

from a patient with a rare genetic cancer pedigree turned out not to be derived from this patient. So I immediately called my collaborators and informed them. You have to set the record straight."

But with respect to H9's parentage, the Gallo team didn't set the record straight until the NIH ordered an investigation.

### V. The Popovic Explanation

Ask Mika Popovic why it took the NIH investigation to get to the bottom of the H9/HUT78 relationship, and he will tell you that he personally investigated this matter over and over again for years until it wore him out. Not only had he tried with Dean Mann to identify the "real HUT78" prior to the landmark 1984 paper, he says, but once the paper was published, "I went back to analyze [HUT78]" with Dean Mann. Because of his doubts about the freezes in the Gallo refrigerator, he says that he wanted to "define which is HUT78 original. But I didn't know precisely where is Adi Gazdar, which is Paul Bunn; I didn't know precisely who is the boss, what is the structure [of Minna's lab], who had consistent contact with Bob Gallo's lab." Just then, according to Popovic, he heard that Paul Bunn "came to seminars and talked about HUT102." So he approached Bunn for cultures, and then describes a great deal of activity: "Dean Mann did several analyses. In addition, I was analyzing H9 banding and the HUT78 which was present in Bob Gallo's lab. And when we got again material from Paul Bunn in the summer of '84, it came out again that those early passages were different HLA types. I must tell you that at that point there were far more important scientific questions in the AIDS research than to precisely pin down whether H9 precisely comes from HUT78. At that point, I told myself: I'm tired of this."



**Wyngaarden on Gallo:**

*"Scientists are kind of at the opposite end of the stream from close management, in general. There are a lot of genetic self-selections that go into the making of a scientist, and there are very few scientists who are green-eyeshade people with respect to balance sheets. And the more creative people like Bob, their minds are constantly working on the scientific problem. In Bob's case, he does that as effectively as any scientist I've ever known anywhere. That's what's being lost in this intensive scrutiny of the fact that he doesn't put the same amount of time and care into the audit side of his work. Now I tend to think that there probably are some major flaws in his record-keeping, in his use of materials—I'm not sure of that, I hope that's not the case—but I'd say the thing to do is to let Gallo be Gallo and to build in a support mechanism. DeVita blocked a lot of that, and you'll hear it from Gallo if he lets his hair down."*

But if that is what Popovic says he did, the following is what he did not do:

He did not try to compare anything in his lab—nor H9 itself—to the samples of HUT78 that existed either in the ATCC or in Adi Gazdar's freezer. Indeed, he made no effort to find Gazdar initially, nor did he try to ask Poiesz, whom he had worked with, about the cells Poiesz had used successfully and left in the Gallo freezer. Nor did Popovic ask Poiesz about the cells Poiesz continued to use successfully in Syracuse.

As for the fresh passages he says he asked Paul Bunn to send over in 1984—the ones he says again proved to be mixed up—Bunn does not recall ever sending Popovic any cells and insists that even if he had somehow forgotten about such a request and had asked for cells to be sent out, there should be a record of it in the Minna lab logbooks, just as there was from 1982. And there isn't.

Popovic also never sought help from any of the NIH scientists who were expert at sorting out cell line mix-ups. For example, he did not approach Stephen O'Brien, chief of NIH's Laboratory of Viral Carcinogenesis and a 10-year friend of Gallo's, who had been involved in sorting out the infamous HeLa cell mess in the 1970s and would play a leading role in the NIH investigation of H9's paternity in 1988. As a relative newcomer to NIH, Popovic may be excused for not knowing of O'Brien, but did he ask Gallo if such expertise existed at NIH? Instead, Popovic depended on Dean Mann, whom he constantly refers to as the "key" person who tried to determine the relationship of H9 and HUT78 with no success. But Mann's recollection and Popovic's are remarkably different on this one crucial point.

Contrary to Popovic, Mann says that Popovic did not tell him until 1988 that he and Gallo wanted to know if H9 came from one of the HUT78 samples. Even in 1984, says Mann, when he was typing H9 along with all the other HT clones, he wasn't attempting to help Popovic compare H9 to the HUT78 freezes, because Popovic never asked him to. "Nobody ever came back to me that I recall and even questioned me as to what the origin of these [clonal] cell lines was," Mann insists. Could he have determined their origin, had he been asked to do so? Easily, Mann told *Science*, if he had an early passage of the authentic HUT78.

Told of Mann's statement, Popovic said only: "He doesn't back me up on this?"

Are such questions about Popovic's actions classic instances of Monday morning quarterbacking? Or was Popovic inflexible in the face of certain challenges? On the eve of the NIH investigation's 1988 resolution of the HUT78 identity question, knowing that such an investigation was about to take place, Gallo ordered Popovic to resolve the matter once and for all. He had asked Gazdar to supply Popovic with some early passages of HUT78. In what now seems an extraordinary moment, Gazdar personally visited Popovic in his lab "to make sure that everything was going along smoothly" with the Gallo team's unofficial investigation. Gazdar recalls that Popovic "showed me this memo from Gallo. It was in Gallo's own hand. It said Gallo expected [the matter] to be cleared up in a paper on his desk in 3 weeks. Popovic just shrugged his shoulders [as if to say:] How on earth after 5 years do I now have [only] 3 weeks to complete this work." So Gazdar inquired as to how Popovic planned to proceed. Then it struck Gazdar full force: "He was going to do

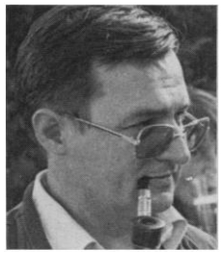
**12 December 1985:** The Pasteur Institute sues the U.S. government, implying that HTLV-III was LAV.

**31 March 1987:** At the White House, President Ronald Reagan and French premier Jacques Chirac officially announce that the nations have agreed on a settlement of the patent dispute.

**10 June 1988:** Crewdson first interviews Gazdar. When Gazdar reports Crewdson's interview to NIH counsel, a little-noticed investigation is begun on orders of outgoing National Cancer Institute chief Vincent DeVita and then National Institutes of Health director James Wyngaarden.

**Fall 1988:** Topic of whether Gazdar had a patent claim is raised by Rabson. Also, according to Mann, Popovic tells him for the first time that it is important to determine if H9 came from HUT78.

**November 1988:** Stephen O'Brien and ATCC establish via DNA fingerprinting that H9 and HUT78 are the same cell line, while Mann concludes the same from another round of HLA typing.



Date: September 6, 1985

From: Mika Popovic, M.D., Ph.D.

Subject: Origin of H9 Cells

To: Chief, Laboratory of Tumor Cell Biology...

"In response to your request concerning the origin of H9 cells and its infection with HTLV-III, I can state the following:

"H9 cell population represents a single cell clone obtained by limiting dilutions from a continuously growing T-cell which we originally thought to be HUT78. In the process of characterization of this cell line and its clones, HLA typing...was performed...and according to the results of HLA pattern, *five* distinct HUT78 cell lines were identified. To avoid confusion we, therefore, designated the cell line susceptible to and permissive for HTLV-III as HT. Since primary non-cultured HUT78 cells are not available, we cannot make a definitive conclusion whether the designated HT cells are identical with the original HUT78 or not. The detailed characterization of the clone, H9, is being prepared for publication and its comparison with HUT78 cells, which will now be obtained from...Dr. A. Gazdar, will soon be performed. In any case, why would anyone care?"

[**Editor's Note:** It would be three years before Popovic finally contacted Gazdar for fresh passages and turned them over to Mann to be compared with H9. The NIH had openly ordered an investigation by then.]

more HLA typing. And I said, 'For God sakes, at least do cytogenetics and then do DNA fingerprinting!' "

That, of course, is what NIH was doing at that very moment as part of an elegant experiment that solved the scientific question but that totally failed to confirm or deny the theories that had been raised for why, as one participant put it, "a lab as sophisticated as Gallo's couldn't handle" a nagging but resolvable question.

### VI. The NIH Investigation

Some of the most controversial theories were reaching the ears of the NIH administrators by 1988. The *Chicago Tribune*'s John Crewdson had begun probing Gallo in every possible way, including filing under the Freedom of Information Act to get Gallo lab documents. Gazdar believes that Crewdson had obtained copies of Popovic's notebooks and had become suspicious that the rumors that H9 came from HUT78 might be more than science gossip. Indeed, Crewdson telephoned Gazdar on 10 June 1988 to ask his opinion. Gazdar says he indicated only that he had no personal knowledge of the facts "but he had heard the rumors too."

But after hanging up, Gazdar decided he had best let his superiors know about the kinds of questions Crewdson was asking. So he reported the call to NIH counsel Robert Lanman and shortly thereafter, Lanman apparently telephoned NCI chief Vincent DeVita who was just about to join Memorial Sloan Kettering. DeVita declined to talk to *Science* on this matter but Gazdar's recollection is that "the next thing I heard was DeVita on the phone in his last month in office saying he was very annoyed at me for not reporting this issue to him rather than having talked to a reporter. I said: 'It wasn't me who talked to the reporter; it was he who talked to me, and I didn't have any facts so there was nothing for me to talk to him about in the first case.' So he said: 'All right, I'm ordering an investigation. I'm putting Al Rabson, [director of NIH's Division of Cancer Biology and Diagnosis—and personally interested in forensic pathology] in charge.' "

But DeVita also telephoned then NIH director James Wyngaarden. As Wyngaarden (who is currently moving from the White House's Office of Science and Technology Policy to the National Academy of Sciences) recollects the conversation, he realized that this was not a trivial problem. Says Wyngaarden, "There was a claim that he [Gallo] had stolen a cell line, essentially, and that's what it really came down to as I interpreted it."

To be fair to Gazdar, there is no evidence whatsoever to suggest that he made any such claim, but it seems more than possible that, in the environment surrounding the controversy over Gallo's use of Montagnier's LAV sample, Crewdson's questions about H9 may have, by the time they filtered up to Wyngaarden, sounded as if another scandal was about to hit the public.

In any case, with DeVita leaving, Wyngaarden took over, setting up a committee of intramural scientists under Rabson's leadership who could look at the two cell lines from an immunological and molecular biological point of view. Recalls Wyngaarden: "Bob thought it was important too. Bob's life is full of controversies and he said: 'Here's one we can settle.' "

And indeed, Rabson settled the matter—at least, scientifically speaking. "It was August '88," he recalls; "Wyngaarden asked me to investigate a very straightforward question: there were three cell lines [that] questions were being asked about. One was H9, the other was HUT78, and the third one was HUT102. The question I was asked in a scientific way was: Is H9 related to HUT78; is it related to HUT102 or is it related to neither of the above? I realized that I could answer this question hopefully very definitely with DNA fingerprinting."

Knowing "from my years in cell culture that things do get mixed up in labs," Rabson remembers setting out to get "the real HUT78, the real HUT102, and the real H9." Enter the ATCC. Rabson asked the repository's researchers to analyze samples of each, without saying why, *and* to supply samples which he turned over for independent experiment to Stephen O'Brien.

O'Brien has had a long and colorful history of characterizing cell lines, uncovering contaminations (he had been involved in decoding aspects of science's most infamous contamination: the one in which human HeLa cells had contaminated and overgrown cell lines that were supposed to be other cell types) and even busting frauds. Gallo had known O'Brien for 10 years, but never thought to turn to him for help with HUT78—something O'Brien says he could easily have done using the technique he developed called allozyme genetic signature.

**17 May 1989:** Gallo finally deposits uninfected H9 in the ATCC.

**June 1989:** The result of the NIH investigation is published as a letter to the editor of a small-circulation journal *AIDS Research and Human Retroviruses*. Yes, it concludes in heavy jargon, H9 is one of many clones that came from HT, which is essentially the same as HUT78.

**19 November 1989:** Crewdson publishes a 50,000-word investigative news article on Gallo in the *Chicago Tribune*. This catches the attention of Representative John Dingell and prompts NIH acting director William Raub to order an inquiry into "cell cultures, motivations, and the like." Also under consideration: whether financial rights have been denied Gazdar.

**8 April 1990:** Gallo is called before a panel created by NIH's Raub in what is to be the first of a series of extended interviews about the controversies surrounding both the isolation of the AIDS virus and the cell line in which it was first grown in quantity.

By 1988 it was a piece of cake for O'Brien: "We had the cell lines and we ran them and the results were unequivocal: the two cell lines [HUT78 and H9] were the same." The third [HUT102] and the fourth [a control] were not. "I remember saying: 'If A were the defendant in a rape case and B were the blood at the scene of the crime, he'd be convicted.' "

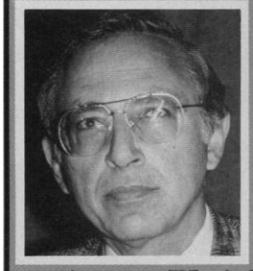
Meanwhile, much the same was happening over at the ATCC. But even that wasn't enough for Rabson, who now decided to "pick two very good scientists outside the National Cancer Institute whom I would ask to just look at the fingerprints: I picked [Richard] Klausner, whom I trust, and Barry Carter, who is a first-rate molecular virologist. It was very crisp. Both labs reported that H9 had derived from HUT78 and was not related to HUT102. I deposited my report and that ended it as far as I was concerned."

Not so for O'Brien, who remembers that he had "the unlucky task of trying to convince Adi Gazdar and Bob Gallo to sign the same paper." This was to be the "Letter to the Editor" that was finally published in *AIDS Research and Human Retroviruses*. "My initial intention," O'Brien recalled, "was to send it as a letter to *Science*." But Dean Mann took the initiative. Mann had become a coauthor by virtue of finally proving the relationship of H9 to HUT78 using his HLA typing on the fresh passages Adi Gazdar supplied. Although Mann says he never has considered the argument about the parentage of H9 important, he says he phoned *Science*. As he recollects it, after he had explained the background of the proposed letter to the Letters editor Christine Gilbert, he concluded that *Science* was uninterested. Gilbert says that she does not remember such a call from Mann, but that she routinely says to callers: "Send it in; we'll look at it," adding that she would have encouraged any letter dealing with a correction of a previous *Science* article, or a controversy concerning Robert Gallo's laboratory.

Whatever actually happened, at that point, according to O'Brien, "Bob [Gallo] said: Dani Bolognesi knows about it. He'll be happy to take it [in *AIDS Research*]. So we sent it down there." Asked if there were any truth to the rumor that Gallo had tried to bury the paper by placing it in a small circulation journal, O'Brien told *Science*: "I will also say that Bob and I did have a conversation about it and he said, 'Look, this is not something worth making a big announcement about and that's what you do when you go to *Science*. I've got enough trouble with this, so I'm perfectly happy to send this to *AIDS Research*. All the people who need to know will see it and that's fine.' "

It was fine, too, for NIH, even though Wyngaarden originally viewed the investigation as responding to allegations that a cell line had been stolen. Wouldn't the finding that, indeed, the two lines were related have tended to bolster such an allegation? *Science* asked Wyngaarden. His response: "Let me see if I can reconstruct this. I never spoke to Gazdar personally, but I think he just wanted something on the record. That's my understanding. I don't think he was making too big a fuss about it. And my recollection is that once the evidence was brought forward that they were probably identical, he had the recognition that he was after and that was sort of the end of it."

Sort of, because within a very few months Crewdson had opened up the whole question all over again in an aside to his mega-report in the *Chicago Tribune*. Gazdar appealed to NIH to consider his rights to income from the Gallo NIH patent. And today, the investigation that never occurred—the one into, as acting NIH director Raub puts it, "the cell cultures, motivations, and the like," as well as the one into the financial deserts of Adi Gazdar—that investigation is now under way. ■ **ELLIS RUBINSTEIN**



## Gallo on Gallo:

*"Maybe I wasn't sensitive enough to somebody's feeling that we should have pursued this to the nth degree but [think] what it was like at that time. There was a tremendous opening to make observations of importance to basic science and to human health. You know, the juices flow, right? Your mind is thinking and moving and you're saying: 'What's the next question?' We discover HIV goes to the brain—we publish it. What's the target in the brain? Microglial cells—we publish it first. How much does this correlate with the dementia in the brain? We tried to establish that. Is the virus present in plasma? We found it was. Is it heterosexually transmitted? We showed that with Redfield. Is it in semen? We showed that with Zagury. When is the virus expressed? When T cells are stimulated. How about more data on proof of causation? We collaborated with people at CDC with the blood transfusion study. What about the genes of the virus: what are their functions? Could we make the blood test better? Can we make an antigen test? We tried, we failed. Are there cofactors? Can we get a vaccine? Can we develop systems to allow Sam Broder and his colleagues to study inhibitors to see if we can help infected people? The pilot studies about AZT were done in my lab by Broder's people. The system that they used was the H9 [cell line] but with more than one virus—eventually a series of viruses. The discovery of molecular heterogeneity was made here by Hahn with Flossie [Wong-Staal] and myself. The discovery of variations within any one virus—what is intra [strain] variation within one individual?—by Mandy Fischer, a post doc now with Richardson in London. Those were important observations for vaccines and for therapy. You have AZT based on some of those studies. You have an opening in Kaposi's Sarcoma based on some others. You have a blood test based on some others. And you have the beginning of a vaccine program, partly at least based on still some other things. I mean, those were the things that were on my mind: get rid of the goddamned virus after you figure out how it works. These are the things I'm still trying to think about. I've got to be worrying and focusing on whether we could have definitely proven in 1985 instead of 1987 that this was derived from HUT78? Maybe so—God knows we were saying it was probable. The fact is that we could have. The fact is that we did tell people we thought that. The fact is I never really thought it was important. And quite frankly, I still don't and I don't understand the people who do."*

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