Vintage Gallo

The tough-guy AIDS trailblazer shares new strategies, old scars and a few surprises

April 1, 1998 By David Gold

Robert Gallo has long been one of the giants in AIDS research. During a 30-year career at the National Cancer Institute (NCI), his lab grabbed the limelight time and again with a trove of dazzling discoveries including Interleukin-2, HTLV-I (the first human retrovirus), HTLV-II and HHV-6 (human herpes virus 6), the first Kaposi's sarcoma (KS) lab model and a new class of body-made HIV inhibitors called beta chemokines. Gallo has also nabbed his share of controversy as the codiscoverer -- along with France's Pasteur Institute director, Luc Montagnier -- of HIV, an event that led not only to Gallo's development of the HIV-antibody blood test but also to federal investigations into his alleged improprieties (based on French claims that the NIH and Gallo "stole" the discovery). Ever the scrapper, Gallo appealed findings of the Department of Health and Human Services (HHS) that he had committed misconduct and claimed victory when HHS declined to challenge his appeal. In 1995, Gallo left the National Institutes of Health (NIH) to form the Institute of Human Virology at the University of Maryland, with start-up funds from the City of Baltimore and the State of Maryland. He serves as its director, pursuing cutting-edge AIDS research on KS treatments, chemokines and therapeutic (as opposed to preventive) vaccines.

In his interview with treatment activist David Gold, Gallo offers an update on his current work as well as some surprising reflections on his career. While researchers typically traffic in careful generalities, Gallo can always be trusted to speak his mind, on the record, like it or not.

David Gold: Worldwide there are now over 30 million people infected with HIV. Did you ever expect this when you began working in AIDS research?

Robert Gallo: No. I was encouraged to work on these cases because our lab had experience in isolating viruses. But I never imagined that this virus would cause so much devastation. Never.

Over the course of the epidemic, you've become a lightning rod for criticism. Why?

It's complex. Part of it is my former personality, which I've tried to bury. And I was working in the government under Reagan, so some people thought I was a Republican. And you had a heck of a press conference [at which thenhealth secretary Margaret Heckler announced Gallo's discovery of the virus, championing it as a triumph for American science]. And of course there was the thing with the French. Heckler gave the French some credit, but she had a cold that day and her voice went hoarse. It all created a bogeyman.

And early on, the gay community [fearful that testing would lead to persecution] didn't understand that the blood test we discovered meant we could grow the virus and test drugs against it. AZT came out of that. I was the co-author, with Sam Broder [former NCI director] and Burroughs-Wellcome, of the first paper on AZT. That work was done in my lab.

In hindsight, what would you have done differently?

If I'd had more confidence in myself, I wouldn't have showed up at that press conference. I'd promised the Pasteur Institute group [the codiscoverers of HIV] that we would make a joint announcement if these viruses turned out to be the same subtype. They were ecstatic. At the press conference, I told a reporter, "Don't call the virus HTLV [the name Gallo had given it]. Very likely, this is going to be the same as the virus isolated last year by the Pasteur Institute [which the French called LAV], so at the very least, call it HTLV3-LAV."

I wasn't a friend of Montagnier. We weren't enemies, but our chemistry is very different -- he's careful in what he says, and I tend to be different -- but I had a friendship with one of Montagnier's researchers, and another worked in my lab. Do you think anybody knew that they had training from us? Or that I provided them with the idea to look for a retrovirus? I also sent them the protocol of how we isolated HTLV-1.

Obviously the French achieved something very important. But what is not known is how we helped in what they did. And what we did in that year was, I think, a considerable amount. And we got killed.

I was never allowed to respond to any single attack by anyone in the media -- whether it be HBO, Sam Donaldson, whoever. Under strict written orders to me, I was not allowed to clarify anything from Rep. John Dingell [D-Michigan, who accused Gallo of scientific misconduct] to HHS or the NIH.

Dingell not only went after you -- he also attacked Nobel laureate David Baltimore.

He also went after Bernie Fischer, the number-one clinical oncologist in America. Fischer just won millions from the government for what he went through. And David's case was particularly awful because some scientists jumped in, in what I think was a totally unethical, malicious manner. Dingell did immense permanent harm.

Did you see how you were portrayed in the HBO movie *And the Band Played On*?

I was compelled to watch the movie by a lawyer who wanted to sue the writers and producers. And I watched it with my family. That was a horror. What can I say?

I had a track record of an honest career, and I had good, young people who were loyal to me and kept me going. And what was the alternative? You either decide to live or you jump into the Potomac. And if you decide to live, you keep pushing forward.

But the NIH didn't abandon me. Maybe they weren't out there slugfesting for me, with the exception of [then NIH head] Bernardine Healy, who was wonderful. She called Dingell "a preposterous fool" in *The Washington Post* and probably got fired as a consequence. But other

than Healy -- who we always said must have bigger ovaries than anyone -- there wasn't anyone out there.

Where do you see AIDS research right now?

We know more about this virus than any other microbe that causes disease. And at last we have practical treatments that benefit people with HIV. But many have failed on these therapies, and it's still too early to know about their toxicity over time. In addition, these regimens are obviously no answer for most of the world's HIV infected.

The pharmaceutical industry can now target viral enzymes and proteins by specific assays in great volume. So they're set for discovering more new drugs. They don't need the academic researchers -- our focus should be on the continued study of the virus, the immune response and how we can manipulate it to make future therapies.

Your lab was the first to propose drugs, such as hydroxyurea, that work against cellular factors rather than the virus itself. Now there are reports of interesting results with hydroxyurea in numerous patients. Can you explain what is different about drugs that target cellular factors?

All viruses, not just retroviruses like HIV, are parasites of the cell. But unlike a bacterium, fungus or real parasite, a virus must be targeted as it's replicating within a cell. In order to reproduce, a virus needs a great number of cellular factors. So we argued that targeting these cellular factors made sense and suggested that hydroxyurea might be useful -- it blocks a key enzyme that HIV needs to make viral DNA from RNA. We weren't pushing hydroxyurea -- we just used it to illustrate the point. And it's cheap, off patent, and any doctor can prescribe it.

What do you think the practical impact of your chemokine research will be for people who are infected now? [Chemokines are natural molecules that prevent HIV from entering the cell. Gallo's lab has identified three chemokines that block particular HIV strains and one that apparently blocks all.]

The whole set of discoveries has opened up extraordinary new knowledge. Every month we know more about how the virus pokes its head through the doorway of the cell, but so far we're just scratching the surface.

Can we use chemokines therapeutically? Obviously, I wouldn't be working so intensely if I didn't think the answer was yes. What about side effects? We don't know. But we've looked at animals, and we don't see much toxic effect, although there may be an inflammatory effect.

But when some chemokines mutate, they lose their pro-inflammatory effects and are still antiviral. So could we use this therapeutically? I would like to. How fast are we making progress? Not as fast as I'd like, which is forever the story. We'll do primate studies -- but we need money for that. These are not the things that NIH funds.

Best case, when could you begin a human trial of these chemokines?

We are speaking with a major biotech company and hope to contract with them, if they can mass-produce it. If it works in monkeys without toxicity, and we can make genetic mutants of it, human studies could begin perhaps within six months. Certainly within a year, if we make the right collaboration.

What is the current state of your KS research?

In 1993 we developed a way to produce KS in mice. Then we found that during early pregnancy, the tumors in mice resolved. We also found that serum and urine taken from humans and mice in the early weeks of pregnancy could destroy KS cells. Then we reproduced these results in mice using an approved drug called human chorionic gonadotropin (HCG), a pregnancy hormone that makes ovaries grow during pregnancy. It is essentially pregnant women's pee, concentrated and purified. About 15 different companies market HCG based on patents from about 40 years ago.

So our colleagues began testing HCG in people with KS. Surprisingly, the results varied based on different preparations of HCG. Though every preparation made ovaries grow, the activity against KS varied enormously. This gave us the clue that the active material was not HCG, but something in it.

Now, at least four labs have published clinical data on HCG. They show that the direct inoculation of some HCG preparations into lesions results in tumor destruction in more than 80 percent of the cases. And using it systemically [bodywide], there have been no toxicities at any dose so far, and 80 percent of treated patients had no KS progression. Of these, 50 percent had partial regression and over 20 percent had complete regression.

Another interesting finding: Some treated patients had reduced levels of HIV and increased CD4 cells -- not every patient and not comparable to that seen with protease inhibitors. And most patients were taking antiviral therapy, so we drew no conclusions. But a few who were off therapy had a documented viral reduction.

These are exciting observations, but I'm very disappointed that we don't know exactly which molecule in HCG is responsible for this activity. We are collaborating with researchers at Columbia University to identify the active molecule and take it into clinical trials.

If you had advanced KS with no other treatment options, would you take HCG?

We still don't know the optimum dose, frequency or route of administration. But if I had KS in an advanced state, you bet your bottom I would be thinking about HCG. I've seen lesions vanish with my own eyes, with no toxicity whatsoever.

The HCG marketed by Wyeth seems to have more activity against KS than the others. But not all batches of Wyeth's product are active. The best dose seems to be 20,000 international units (IU) of Wyeth's HCG, three times per week, either by intramuscular or subcutaneous administration.

Do you think that human herpes virus 8 (HHV-8) is the causal agent of KS?

I don’t buy that -- yet. After all, 80 percent of Japanese people are infected with HHV-8. I’m not saying it’s not involved in augmenting KS, but there’s absolutely zero evidence that this is a tumor virus.

What is your current thinking about human herpes virus 6 (HHV-6), which your lab discovered?

We need a specific drug for HHV-6, because we think it’s involved in late-stage AIDS progression -- in some people. In the test tube, that bugger kills T-cells very well.

Can you describe the difference between doing AIDS research inside and outside of government?

Being outside gives me more freedom and the ability to bring things to the labs and the clinic. I should have done this 10 years earlier. Of course, the bad part is that it takes a tremendous amount of time to raise money.

What should the NIH be doing differently in terms of funding AIDS research?

Researchers are forced to spend too much time on these fucking grants. It drives you nuts. There’s far more politics than I was expecting. And I worry about the competence of the review panels. Quite frankly, I’ve never heard of two-thirds of the people on these panels. But when you criticize the NIH, they ask, “Would you sit on a review committee?” The answer is “No, of course not -- I’m too busy.” Why would I want to sit there, going through everybody’s books?

We need a mechanism to help fund practical, novel, clinically oriented pilot studies. Why the fuck do I have to spend 10 years to get small amounts of money to be able to go to the next step? Why the hell can’t that be done fast?

Last year, you were widely quoted as saying that a vaccine may not be possible. Is that still your feeling?

That was a misquote. Back in 1984 I thought we’d have a vaccine in a relatively short time. But since 1986, I’ve said we may have a vaccine tomorrow, in 10 years or never. Now we have some vaccines that are partially effective in animals. I hope they’re effective in humans.

Some people have suggested that we should dramatically retarget research toward developing a preventive vaccine. But I fear too rapid and premature a change toward preventive vaccine research. The current therapies are not the end of the problem. And we can’t just write off millions of people who can’t afford these drugs or have failed them.

You’ve been outspoken in opposing human trials of live HIV vaccines. Why?

I strongly believe that there are great risks in testing a live HIV vaccine. The proponents of these trials have absolutely no idea what the risks are. My experience is that most animal retroviruses that replicate can ultimately produce disease. So in 20 years, the live vaccine could cause AIDS in many of those vaccinated.

Several times I've asked that the live vaccines be tested in monkeys whose immune systems are activated, because in Africa a lot of people have activated T-cells due to infections with different pathogens.

Do you believe it is feasible to eradicate HIV from the body?

In theory it is. You don't need complex math to figure out that if you suppress virus to zero for long enough, the other cells will die of old age. But no one knows the lifespan of some of those reservoir cells. And there's not enough time to know that there won't be secondary effects with long-term chemotherapy against the virus. Therefore any attempt to say that is just not based on hard science.

It's good to put things out there and stretch the field as far as you can. But we just don't know how long these cells live. And I don't know anyone who has yet achieved 100 percent virus suppression.

What about stimulating the immune system to "flush out" the remaining virus? Does this make sense?

Yes and no. We are exploring a couple of ideas in this area. But Daniel Zagury's lab has demonstrated that it's difficult to stimulate the immune system in people with HIV because of the relative anergy [paralysis] of the uninfected T-cells. So we are working on targeting the HIV tat protein and reducing levels of alpha interferon, preferably in combination with antiviral therapy. Hopefully, we will then be able to overcome the anergy of the uninfected T-cells and stimulate the immune system.

Bottom line, do you think that five years from now we're going to be treating this disease in different ways with significantly better results?

Yes, I think we'll have more drugs and more types of approaches, particularly biologic ones. But the enormous uncertainty is whether there will be a patient population to adequately test new approaches on. And whether the ethics will allow it. But this gets into non-scientific problems, where I lose my intuition.

People may say, "You can't try that approach -- you have to use triple-drug therapy along with the new therapy being tested." So you'll end up only being able to test new therapies on those with the most advanced AIDS, where they may have limited efficacy. It could really slow down the study of new therapeutic approaches.

How would you test new agents on asymptomatic patients who are taking triple-combination therapy and have essentially undetectable viral loads?

I wouldn't do it at that stage. I'm not going to say, "I'm sure we have the answer, so don't use existing anti-HIV therapies." I was thinking more in terms of testing these things in countries where people don't have the money to do triple-drug therapy. But it may get very controversial. Even if a new approach cured monkeys, it wouldn't matter, because it's not ethical if you don't give triple-drug therapy. I find fault with that kind of ethics. But it will be thrown at us. So we could

end up only testing new approaches on people who fail everything else. That may not be a fair test, and we may never know if these drugs work.

Many people who know you say that although you mean well, you speak out when you shouldn't. For example, last year, in a *Wall Street Journal* article on David Ho, you said, "There seems to be an awful lot of press releases coming out of that lab." Why did you say that?

I don't know. It just came out. The reporter told me that Ho's lab said they were being treated unfairly by the media, which was saying too many things about their work. And I said, "Oh yeah, why do they make all these releases, then?" That's what I said. He didn't misquote me.

So that was a problem. My mother always said, "That thing in the middle of your face is going to get you into trouble." And she meant my tongue. But I'm learning.

Is the competition between top researchers useful?

There is no question that competition is important and useful in science. As science gets better and better, you strive to do better in order to excel. But I am not the same person I was 20 years ago. I have a far more philosophical outlook. That comes with age, time and the experience I went through.

And I can tell you with every molecule in my body, I get great pleasure when I read a good original scientific paper. It's marvelous to see. But 20 years ago my reaction would have been "Jesus Christ, why didn't I think of that?"

Hatchet Job?

In a bizarre e-mail that reveals one researcher's strong feelings about Gallo, John Moore, of the Aaron Diamond AIDS Research Center (ADARC), claimed recently that Gallo was conspiring to "get" his institution. The ADARC researcher alleges that Gallo phoned the two scientists who, along with Gallo, are credited with discovering HIV -- University of California researcher Jay Levy and French researcher Luc Montagnier -- "solely to ask them to bury the hatchet so we can combine forces to get the ADARC crowd." Moore labels such behavior "sick and twisted."

All three star scientists deny the allegations. According to Montagnier, the story is "absolutely untrue. It never happened." And Levy says that "the story is garbage. No such thing ever occurred." For his part, Gallo dismisses Moore's version as "ludicrous." "In all my life," he says, "I've never even contemplated the possibility of doing that to anybody. It is a slanderous charge. I may disagree with David Ho on some specific scientific theories. But I would never try to damage him or his lab in any way."

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Many Fans, One Foe: What the Pros Say About Gallo

David Baltimore, president, Cal Tech: "The world owes Gallo for undertaking the search for the cause of AIDS when most others refused to be drawn into it. He co-discovered the virus, was the

first to make it in large amounts and develop a test for it. His recent work on chemokines is a key step in the realization that the chemokine receptor is part of the virus entry machinery. And he's done lots else.

If Bob had been an understated, shy man, he'd now be universally recognized as a hero. The witch hunt he suffered was a horror show, and he got surprisingly little support from the scientific community. He deserved better and it was wonderful that he was ultimately exonerated."

Larry Kramer, author, activist: "Gallo is fabulous. He never stopped in his research efforts, despite horrific attacks by that evil congressman John Dingell and others. He rose above it all and continued to come up with a series of brilliant discoveries of immense benefit to people with AIDS."

Martin Delaney, Project Inform: "Bob Gallo's an extraordinarily bright and intuitive scientist. He has the insight and the ability to make leaps of logic and be right. He also recognizes that intense chemotherapy may not work over the course of a lifetime and is a leader in seeking new therapeutic approaches. His work on chemokines may ultimately change the game in AIDS research."

Anthony Fauci, National Institute of Allergies and Infectious Diseases: "Gallo is a truly outstanding scientist. What makes him so unusual is that he's brilliant, has an incredibly creative mind and is able to keep his eye on the ball. That is, he stays focused on the practical side of research. There's no doubt that he is extremely competitive, but he's also a very warm, generous guy."

Beatrice Hahn, University of Alabama, Birmingham: "Never underestimate him as a scientist. He is very flamboyant and quite an interesting character. He has remained extremely productive over the years and was furious over reports that he was considered 'old wood' and that a young generation was taking over. Why do people have such strong feelings towards him? Because he has such strong feelings about others and usually doesn't hesitate to express them."

Steve Miles, UCLA School of Medicine: "Gallo is the most dominant intellectual force in HIV medicine, bar none. Most of us would love to accomplish any one of the many discoveries he's made in a lifetime. Gallo did all that and will do more. There is simply no one else in the field of HIV that intellectually compares to him."

Luc Montagnier, French researcher, World Health Foundation: "We are very different, and we've had our differences. But we have similar visions in terms of AIDS research. We both approach our research with great enthusiasm and have been working on this disease from the very beginning, while others have come and gone."

John Moore, Aaron Diamond AIDS Research Center: "He is grossly overrated as a scientist. If you are dumb enough to believe Gallo's personal propaganda, that's your problem. But it reflects badly on your competence as a journalist if you swallow his line and waste print space on him. And if you think Gallo had much to do with the chemokine work, you are a fool."

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http://beta.docker.poz.com/article/Vintage-Gallo-1608-4332