

A Historical Summary of Dr. Robert C. Gallo

Past

Gallo began searching for human retroviruses in 1970. After reverse transcriptase (RT) was discovered (by D. Baltimore and the late H. Temin) in retroviruses of animals, Gallo and co-workers began to refine RT assays so that assays of it could be used as a sensitive and specific marker for a putative human retrovirus (numerous publications in the 1970s and reviewed in [ref.1](#)). In order to do so, he and his team focused on methods to distinguish virus RT (a DNA polymerase) from the three DNA polymerases of human cells. This work was undertaken at a time of generalized and strong resistance in the scientific community to the idea of even the possibility of existence of any human retroviruses ([2](#)).

Believing that to identify and isolate a human retrovirus he would have to be able to grow primary human cells (more specifically various kinds of blood cells because he was looking for a virus associated with one or more kinds of human leukemia), Gallo began to search for specific blood cell growth factors. Initially, he and his co-worker (R. Gallagher) found a human embryonic factor which induced growth of myeloid (granulocyte lineage white blood cells) and used it to establish the first human myeloid leukemia cell line (HL-60) with his post-doctor S. Collins ([3](#)). However, they had no success in finding bona fide human retroviruses.

In 1976 he and his first year post-doctoral fellow, D. Morgan, (later joined by F. Ruscetti) found a factor released by T-cells that promoted growth of other T-cells ([4](#)). In 1977, with Ruscetti and Morgan they better described this system. They called the factor T-Cell mitogenic factor later termed T-cell growth factor ([5](#)) (TCGF). Gallo and J. Mier, another post-doctoral fellow, purified the factor in 1980 ([6](#)). Subsequently, others renamed TCGF as Interleukin-2 or IL-2, one of the first cytokines to be discovered, and a growth factor which would soon be seen as essential to the subsequent discovery of all human retroviruses and also eventually used in treating some cancers.

In 1980, Gallo and his first-year post-doctoral fellow, B. Poiesz, applied IL-2 to leukemic T-cells and isolated human T-Cell leukemia virus -1 (HTLV-1) ([7](#)). This was the first human retrovirus and the first human leukemia virus. Gallo and his colleagues published five papers between 1980 and mid-1981 ([7-12](#)) before Japanese workers made their isolation of the same virus ([13](#)). Work by Gallo's team and independent work in Japan showed that HTLV-1 was the cause of the particular leukemia first described by K. Takatsuki in Japan known as adult T-cell leukemia or ATL which is highly prevalent in parts of Japan and sporadic in most of the rest of the world ([14A](#), [14B](#)).

In 1982, Gallo with his post-doctoral fellow, V. Kalyanaraman, discovered HTLV-2, a second leukemia virus, which was not nearly as pathogenic as HTLV-1, being associated only with unusual variants of the leukemia known as hairy cell leukemia ([15](#)). Additionally, in this period European scientists discovered that HTLV-1 also caused a serious and sometimes fatal neurological disease often previously confused with multiple

sclerosis. It is also about this time that Gallo and his group developed a blood test for HTLV-1, which much later (following his HIV work and blood test) was made a required blood test in Japan and in the U.S. (circa 1988 – 90). HTLV-1 is endemic in substantial portions of Japan and infects a significant number of African Americans. Otherwise, it is a sporadic and unusual infection in other U.S. populations and in most other regions of the world.

Thus, before his HIV work, Gallo made huge contributions to public health by defining one of the first demonstrated infectious causes of a cancer and developing a blood test for it.

AIDS

The HIV/AIDS epidemic is the greatest pandemic in contemporary history and one of the greatest of all time, to date killing more than 40 million people while more than 30 million are now infected. HIV/AIDS is a destructive and destabilizing force for numerous underdeveloped nations even, having impact on the security of other nations. It alone, has contributed to a marked rise in orphans. Additionally, HIV greatly increases the spread and virulence of TB and many other infectious diseases.

In May 1982, Gallo became enticed to study AIDS, and in that year Gallo and M. Essex of Harvard's School of Public Health were the first to propose that AIDS was most likely caused by a new human retrovirus. Gallo was stimulated toward this idea by his experience with HTLV-1, which was transmitted from one person to another by blood, by sex, and by mother to infant. This fit with the information being accumulated by the Centers for Disease Control (CDC) on the risk groups for AIDS. Further, Gallo knew HTLV-1 and HTLV-2 targeted CD4 T-cells, and U.S. clinicians describing patients with AIDS, reported a decline in CD4 T-cells (2). The technology developed for HTLV-1 and the acceptance by the scientific community now of the existence of human retroviruses hastened Gallo's group to go after a retrovirus in AIDS - as they did for the Paris group, headed by L. Montagnier. Though the Gallo/Essex idea was the only productive hypothesis, it was not exactly correct, because although HIV is a retrovirus and shows many similarities to HTLVs, it is not in the HTLV retrovirus "family" but is in another retrovirus family (16).

In 1983, the L. Montagnier/Chermann group reported on a new retrovirus obtained once from a man with lymph gland enlargement (17). They later called the virus LAVbru (lymphadenopathy from patient bru). Gallo had given the French their first IL-2 and the T-cell growth protocol to culture the T-cells from this patient. Incidentally, F. Barré-Sinoussi, the assistant to Chermann, worked in Gallo's lab for a few months in 1982 to further learn lymphocyte culture techniques. Gallo also provided antibodies to HTLV-1 and HTLV-2 in order that the Paris group could distinguish what they had from the HTLVs (acknowledged in their 1983 paper). Their paper was first rejected by *Nature* magazine. Montagnier and Chermann then discussed this with Gallo who called *Science* magazine to tell *Science* editors he (Gallo) believed this paper was correct and should soon be published. *Science* agreed and asked Gallo to review it. Gallo reviewed it within

one day and he said it should be accepted for publication, and it was. This is documented with copies of the letters (18).

During the same year (1983), Gallo and his group obtained many independent isolates of this new retrovirus from AIDS patients. Prior to submitting their papers to *Science* and *Lancet* in March 1984, they obtained 48 isolates of the retrovirus (19) and at first called it HTLV-III, to designate it as the third now known human retrovirus. This was in keeping with an international nomenclature agreement at Cold Spring Harbor in September 1983 (18). Soon after, a group met to designate the generic name to these virus isolates as HIV.

In the fall of 1983, M. Popovic and Gallo made a significant breakthrough. They learned how to continuously grow HIV in permanent culture in immortalized T-cell lines (20). This too was published as one of the five papers (20) submitted to *Science* (4 papers) published in May 1984 and the fifth in *Lancet* (June 1984). This advance led to the possibility of an accurate and sensitive blood test (also published in *Science* May 1984) (21, 22) and in *Lancet* (June 1984) by Safai et al (23).

The blood test was the first practical advance in HIV/AIDS research, and it was a major one because:

1. It preserved the blood supply for much of the world literally saving millions of lives and greatly reducing the size of the epidemic;
2. It allowed the epidemic to be followed for the first time since previously physicians and public health workers had to wait for signs of AIDS which usually developed only after five to ten years from the time of infection, whereas the blood test would be positive within a few weeks of the time of infection. Consequently, physicians and healthcare workers could intervene with educational programs, and when therapy became available, it could begin early – much before it was too late;
3. Finally, it greatly aided in linkage of HIV to AIDS as its causative agent because science requires verification and few investigators then had the tools and/or experience to obtain many independent isolates of HIV in culture from patient's blood cells (which at the time was also seen as a great risk to the researcher). Also, when AIDS developed it was generally associated with many opportunistic infections, providing results to convince scientists that this one new retrovirus was the single cause of AIDS was not easy, but that is what Gallo and his group did and did so rapidly. The great physician, Sir William Osler said: it is not who makes a point first but rather who moves the scientific community. That only occurred in May 1984 from the work of Gallo and his team.

Meanwhile, the Montagnier/Chermann group reported some additional isolates of the new retrovirus (described in the Cold Spring Harbor meeting in September 1983 and published in 1984) (24). However, they then believed that the retrovirus they first found (“LAV”) was linked to lymph gland enlargement, whereas their recent isolates (of HIV) found in AIDS cases were different, and they called the latter IDAV1, IDAV2... for immune deficiency viruses. They also hypothesized in this (their second paper) that

HTLV-I and II might also cause AIDS, which of course was wrong – there being only one single cause of AIDS. Thus, there was clearly back and forth progress with one group leaning on the other for awhile and vice versa.

Troubles began in 1985 with patients for the blood test. The National Institutes of Health (NIH) had not patented before (as they regularly do now) but the blood test was their initial foray into this legal world as it was for Gallo. The U.S. Health and Human Services stated that the patent was to protect against fraudulent use of blood tests, and to entice larger companies to come in and work on the problem by giving semi-exclusive rights. The Gallo group won all rights both in Europe and the U.S. Though the Paris group patented earlier, they could not reduce the findings “to practice,” chiefly because they could not continuously grow HIV, whereas the Gallo group succeeded with 6 of the original 48 HIV isolates growing in continuous culture (20). Consequently, the Montagnier patent had only 17% of AIDS patients positive in their test, whereas the Gallo group had from 88% to 100% in tested coded “blinded” samples (18, 21, 23).

When in 1985 discord was accelerating, Gallo and Chermann wrote a history of co-discovery based on the Montagnier/Chermann earlier publication on LAV and Gallo’s earlier and necessary contributions of the T-cell culturing technology, the RT assay, the HTLV antibodies and the idea that AIDS would be caused by a retrovirus, as well as the later linkage of HIV to AIDS by multiple HIV isolates and the blood test. However, Gallo was telephoned by Madame C. Escoffier-Lambiotte, the medical science editor of *Le Monde* with the request that he not (ever) use this history because it would destroy the career of Gallo’s friend J.C. Chermann, at the Pasteur Institute (this would have interfered with the plans of the lawyers in New York representing the French government and the Pasteur Institute who were planning on legal action to gain some of the patent royalties).

It was in this period that Nobelist and President of the Pasteur Institute, F. Jacob, met for dinner with Gallo and D. Zagury of the University of Paris in the home of C. Escoffier-Lambiotte. Jacob asked Gallo: “Do you believe Pasteur deserved some of the money?” Gallo answered yes. Jacob said “you (Gallo) have the power to get a portion for us.” Gallo felt he did not but would try. Jacob stated he did not want to hurt Gallo but warned him if he didn’t succeed then actions would move to the Board of Pasteur composed of business men and lawyers, and they would be very tough, including the use of media and other actions.

“The Contamination” Allegation

In 1988, agreement did occur between Pasteur Institute and the French government, and Gallo and Montagnier decided to write a joint history of respective contributions as co-discoverers published in *Nature* (25). For awhile, all was well. However, by the following year more vicious attacks occurred emanating from the New York lawyers who felt inadequately paid. Their attacks and contacts brought in a close relationship between them and U.S. (Michigan) Congressman John Dingell, who at the time was going after U.S. scientists, most recently then Nobelist David Baltimore, as well as several others

which brought him publicity (the latter, 8 of 8 scientists were found guilty of nothing) (18). Using Dingell and a writer (J. Crewdson), the attacks went on for more than four years, and virtually removed the most active, prolific, and needed researchers essentially out of research. The focus was that despite the tremendous public health success of the blood test, Popovic/Gallo used “the French virus – LAVbru.” As noted, Gallo/Popovic had several HIVs in culture, but they chose that one because it had the highest titer. Indeed, it was cross-contaminated with virus from the French, so another agreement was made to give still additional funds to the “French.” However, in 1991, Gallo’s team obtained original material from patient bru (the source of the LAVbru strain of HIV from the French), and the Gallo team (headed by M. Reitz in this study) found that LAVbru was a completely different virus, which as the French stated, could not (and to this day has never) grown in a cell line continuous culture (26). In fact, LAVbru was sent to Gallo’s team a few times and they confirmed it could not grow. So, what happened? The French group reported confirmation of this result (27), but explained that an HIV strain from another patient (LAI) first contaminated their culture, but they were unaware of that when they sent the last shipment of what was supposed to be LAVbru. They had instead sent LAI. Popovic could not have known this nor could he have been able to suspect that the virus of the Popovic/Gallo culture came from the French.

It is sometimes written that “Gallo was found guilty by the Office of AIDS Integrity (ORI)” but the charge was later dropped. It should be known that after 4 years of three scientific committees, Gallo was never found guilty of anything by these committees. ORI is composed of administrators and lawyers, not scientists, and their spokesman later acknowledged in an interview published in *Science* magazine (18) that they were “damned if they did (find Gallo guilty because there was nothing) and damned if the did not (because they were under pressure from Congressman Dingell).” Again, it is noteworthy that Dingell went after 8 notable scientists and all 8 were innocent in the end (18). The temporary “guilt” (of about three weeks duration) for Gallo had nothing to do with the work with HIV, rather after reviews of innumerable Gallo publications in a malicious attempt to find something wrong, it was over a half of a sentence in one publication that had an arbitrary interpretation. In short, they had to get something on him. It is true that Popovic was found guilty by one science committee, but again not for the “French virus” but over a trivial portion of a Table in the paper he was the first author (20). He said ND meant the result of a certain experiment was non-determinable. ORI said it always meant an experiment was Not Done and since Popovic did the experiment this was false, hence falsification! This too was dropped as Popovic proved them wrong. Most important of all was the final analyses done by an impartial group to make a final decision. Their executive summary conclusion stated: “After all the sound and fury one would have expected to find some iota of evidence of wrong-doing. There was none” (18). These events also ended with Gallo and Montagnier writing more papers together (*Scientific American* – 1988; *Science* 2003; and *New England Journal of Medicine* 2003) (28-30).

From 1984 – 85, in a notable series of publications Gallo, and his group and collaborators sequenced the entire genome of HIV, characterized several of the HIV proteins, contributed to our knowledge of the novel HIV regulatory genes and protein, discovered

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virus in the brain, saliva, and semen, along with clinical collaborators (J. Groopman and R. Redfield) first showed HIV was also heterosexually transmitted, discovered variations of HIV from one isolate to another and microvariants even within one isolate (one patient), carried out numerous worldwide sero-epidemiological studies and demonstrated that macrophages, not only CD4 and T-cells, were also targets of HIV (see papers collected by *Science* editor R. Kulstad) (31).

The system of continuous T-cell line culture developed by Popovic/Gallo was quickly used (1986) by S. Broder and his co workers, H. Mitsuya and R. Yarchoan, in their development of an objectively effective anti-viral therapy for the first time in the history of medicine (32). This soon led to the development of the triple drug therapy by bringing the pharmaceutical industry into the problem, which in turn led to the dramatic improvement and longevity of HIV/AIDS patients. Meanwhile, Gallo's blood test (available by the spring of 1984) reached the bulk of industrialized nations by January 1985, the exception being France which delayed use of the blood test for almost one year so they could have their own test (which in fact was mainly developed for them by the U.S. company, Genetic Systems). This cost many lives (18).

In 1986, Gallo and co-workers D. Ablashi and Z. Salahuddin discovered human herpes virus-6 (HHV-6) (32). This was the first new human herpes virus to be discovered in more than 25 years. Later, Japanese workers showed it was the cause of a febrile infant disease and sometimes serious, a disease of infants called Roseola infantum. Others today suspect that HHV-6 plays a role in some neurological diseases.

In 1995, Gallo and his group reported the discovery of the first natural inhibitors of HIV, a subset of molecules known as Beta Chemokines (33). This in turn helped lead to the discovery of the HIV co-receptors which are also the receptors for these chemokines.

Present & Future

In 1996, after 30 years at the National Cancer Institute (NCI) of NIH, Gallo left to form the Institute of Human Virology (IHV) of the University of Maryland School of Medicine, in Baltimore, Maryland, where he is still the Director. Along with co-founders William Blattner (also from NCI) and Robert Redfield (from Walter Reed in Washington, DC) they formed an Institute composed of divisions of basic research-vaccine (Gallo and G. Lewis, Co-Chair), epidemiology-public health (W. Blattner, Chair), clinical (R. Redfield, Chair) and animal models (J. Bryant, Chair) – under one roof and focusing on HIV/AIDS. When arriving at the University, 200 HIV/AIDS cases were followed, but this was quickly increased to more than 5,000 by an outreach program to the inner-city African-American population. The clinical research program aims at finding ways of making some currently used anti-HIV drugs work better. Both the clinical and the epidemiology divisions obtained the President's Emergency Program for AIDS Relief (PEPFAR) funding to help train doctors and other healthcare workers to care for and treat HIV infected people in underdeveloped countries. Currently, IHV is involved in 7 African and 2 Caribbean countries and treating more than 350,000 patients and following several hundreds of thousands more. About 11% of all African patients treated today are

under IHV's PEPFAR programs. Gallo is also currently trying to convince the U.S. government leadership to include "Inner-City U.S.A." as one of the PEPFAR countries (now at 15 – most in Africa) since African Americans in the inner-city of several regions of the U.S. have infection rates not dissimilar to some of these developing countries.

The vaccine division of IHV has an exciting HIV vaccine candidate that has had demonstrable potency and breadth in primate animal model studies (34). Gallo and co-workers A. DeVico and G. Lewis are now trying (with the help of the Gates Foundation) to find a way to increase the time of immune response. If found, this would open the way to clinical trials.

Recognition\Awards, Etc.

Gallo has published close to 1,200 scientific papers. He was the most cited scientist in the world from 1980 – 1990 (35) and ranked third in the second half of the twentieth century in "impact of discoveries" (36). He is a member of the U.S. National Academy of Sciences (1988—present) and the U.S. Institute of Medicine of the National Academy of Sciences (1989—present). He is the recipient of 27 honorary degrees, including three from Israel. His major prizes include the following: uniquely he has received the U.S. Albert Lasker Prize twice (1982 for cancer and 1986 for HIV/AIDS); he has also received the U.S. General Motors Cancer Research Award (1984); the American Cancer Society Gold Medal of Honor for Cancer Research (1983); Spain's Prince Asturias Award (2000); Canada's Gairdner Prize (1987); Germany's Paul Ehrlich and Ludwig Darmstaedter Award (1999); Japan's Science & Technology Award (1988); Italy's Tevere Prize (1983); France's Griffuel Prize (1983), the World Health Award from M. Gorbachev (2001); and Israel's top prize, the Dan David Award (2009), and many others, including recognition for cancer research from Tel-Aviv University (Otto Herz Award) and for immunology research from Hebrew university (Rabbi Shai Shacknai Prize). He was also elected to the Inventors Hall of Fame in 2004.

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