is the immunodeficiency that allows non-pathogenic microbes to become killers and other latent microbes to multiply. Pneumocystis pneumonia caused by \textit{P. carinii} is rare in immunocompetent people but common in patients with AIDS; yet, \textit{P. carinii} is not the cause of AIDS. KS, a rare cancer in immunocompetent people but frequently seen in AIDS patients, is caused by human herpes virus 8, also called KS-associated herpes virus (KSHV), which is transmitted sexually but remains latent in immunocompetent people (18, 19). Clearly, neither KS nor KSHV is the cause of AIDS. About 10\% of people infected with HIV also carry HTLV-I, the first human retrovirus causing cancer to be identified (9, 10, 13). Thus, the demonstration that HIV causes AIDS was no small task.

I have suggested to Gallo that the scientific process might well be served if he and Montagnier were to write somewhat different accounts of how the cause of AIDS was discovered. Although Gallo and Montagnier tried to do this (20, 21), the need for each to be called the codiscoverer of the AIDS virus prevented resolution of the scientific dispute. The codiscoverer status had been a political solution devised by U.S. President Ronald Reagan and French Prime Minister Jacques Chirac in their attempt to resolve the dispute over patent rights central to prepare a hepatitis B vaccine might have been contaminated by the AIDS agent. On 3 January 1983, François Brun-Vezinet obtained a lymph node biopsy from one of Rozenbaum's patients, a young gay man (BRU) with a lymphadenopathy in the neck. I mixed the lymph node, dissociated the fragments into single cells, and cultured the T lymphocytes with interleukin-2 and antiserum to human interferon. Françoisine Sinoussi (by then Barre-Sinoussi) and her assistant Francoise Barre-Sinoussi prepared the virus family as Montagnier's LAV and Gallo's HTLV-I, all later renamed HIV (19).


I thank F. E. Cohen, A. Gallo, M. Koprowski, J. Levy, L. Montagnier, and N. Nathanson for helpful comments, and M. Nguyen for help with the manuscript.

References and Notes

7. Levy called the virus that he isolated AIDS-associated retrovirus or ARV (13), which turned out to be from the same virus family as Montagnier's LAV and Gallo's HTLV-I, all later renamed HIV (19).
12. I thank F. E. Cohen, A. Gallo, M. Koprowski, J. Levy, L. Montagnier, and N. Nathanson for helpful comments, and M. Nguyen for help with the manuscript.
received a biopsy from another young gay male patient (MOI), who was infected with both HTLV and the new lymphadenopathy-associated virus. If MOI had been our first patient, we would have been very confused.

A few months later, I received a blood sample from a young hemophiliac (LOI) with full-blown AIDS, and blood and lymph node samples from a young gay man (LAI) with advanced Kaposi's sarcoma. The LAI virus could be isolated from the patient's blood cells and grew very quickly in the patient's cultured T lymphocytes, killing them as well as killing T lymphocytes from blood donors. In September, we isolated a similar virus from the blood of a Zairian woman, ELL, who died of AIDS a week later. All of the isolated viruses showed cross-reactivity between their gag proteins (p25 and p18) (5). The viruses isolated from full-blown AIDS patients were more aggressive than the BRU virus, and so I called them immune deficiency-associated viruses (IDAV). The viruses like BRU that were isolated from patients who only suffered from lymphadenopathy were termed lymphadenopathy-associated viruses, or LAV. This classification corresponded to the later terminology of syncitium and non-syncitium-inducing strains.

The retrovirus was new, as was the disease. My collaborator, the electron microscopist Charles Dauguet, showed me pictures of the viral particles whose dark, cooly-shaped centers suggested that this virus was not the same as HTLV. The molecular biologist Edwald Edlinger suggested that I compare the new virus with animal lentiviruses, and, indeed, the pictures of viral particles we obtained in June 1983 looked identical. As I told Robert Gallo, I was convinced that we were dealing with a virus quite different from the HTLV family.

To better characterize the new virus, we tried (unsuccessfully) to grow the BRU isolate in different T cell lines. If we had tried the LAI isolate instead, we would have been able to grow the virus without any trouble. In October 1983, we were finally able to grow the BRU isolate in Epstein-Barr virus-transformed B cell lines, although we discovered later that the LAI virus had contaminated our BRU culture (6). At least six laboratories received the LAI sample (under the name BRU) from our group and experienced the same contamination. We think that the LAI virus readily contaminated the BRU culture because it associates with a mycoplasma species, Mycoplasma pirum, usually present in T cell lines. This physical association makes a fraction of the LAI virus highly infectious, and, in fact, this fraction can be neutralized with antibodies against M. pirum. As mycoplasmas are common contaminants of cultured cells, an infectious prototype virus (LAI associated with M. pirum) may have caused several contaminations between 1983 and 1984 in different laboratories.

New evidence that this strange retrovirus was the cause of AIDS came from our team in the fall of 1983 and the winter of 1984 (7). We observed a high frequency of antibodies against the virus in lymphadenopathy patients, and noted the favored tropism of this virus for CD4+ T lymphocytes. Our results were still controversial, however, and we had difficulty in obtaining the funding needed to better characterize the virus and to develop a blood test. The tide only turned in France when Robert Gallo and his group in the United States made a similar discovery. In the spring of 1984, Gallo published more convincing evidence that HIV caused AIDS (8) (see the Viewpoint by Gallo on page 1728), a finding that was confirmed by Jay Levy's group (9). In 1985 came the cloning and sequencing of the HIV genome with identification of new open reading frames specific for lentiviruses (10). This was followed by identification of the HIV large surface glycoprotein (11) and of T cell CD4 as the receptor for HIV (12, 13). In 1986, HIV-2 was isolated from West African patients (14).

Over the past 20 years, the scientific and legal controversies between our team and Gallo's group have faded. We are left with the salient fact that HIV was identified and shown to be the cause of AIDS less than 2½ years after this disease was first identified. It took only another 2 years for blood tests to become commercially available, reducing almost to zero the transmission of AIDS through blood transfusion in developed countries. In 1987, the first anti-HIV drug, AZT, which blocks HIV RT activity, was introduced. With the arrival of the HIV protease inhibitors and triple drug therapy in 1995, many patients are alive today who would otherwise have died.

But we must not be complacent—the task ahead is immense. We still do not understand the origin of the AIDS epidemic; the slow destruction of the immune system; factors which determine HIV infection of CD4+ T cells; the importance of cofactors in AIDS progression and virus transmission; and the nature of the HIV reservoir that resists triple drug therapy. The next wave of advances in the fight against this worldwide scourge will require the contribution and energy of us all.

References and Notes

VIEWPOINT: HISTORICAL ESSAY

The Early Years of HIV/AIDS

Robert C. Gallo

Animal retroviruses were among the earliest viruses discovered, and by the 1960s some were shown to cause cancer. These findings prompted the formation of the U.S. Virus Cancer Program, which aimed to identify human tumor viruses, especially human retroviruses. By the late 1970s, however, a mistaken consensus emerged that viruses did not cause human cancer and that human retroviruses did not exist, leading to termination of the program. Even more perplexing was the assertion that serious epidemic diseases were limited to the "Third World," culminating in the closure of certain U.S. medical school microbiology departments and a disturbing lack of support for the U.S. Centers for Disease Control and Prevention (CDC). In the midst of this complacency, my co-workers and I made human retroviruses one of our primary research objectives. We were interested in leukemia and began to characterize the DNA polymers in blood cells (1, 2). Howard Temin had proposed that retroviruses replicate through an integrated DNA intermediate, a notion supported by his discovery of David Baltimore of a retroviral reverse transcriptase (RT).

This discovery provided me with an entry point into the field because RT is a DNA polymerase. We developed sensitive assays to detect