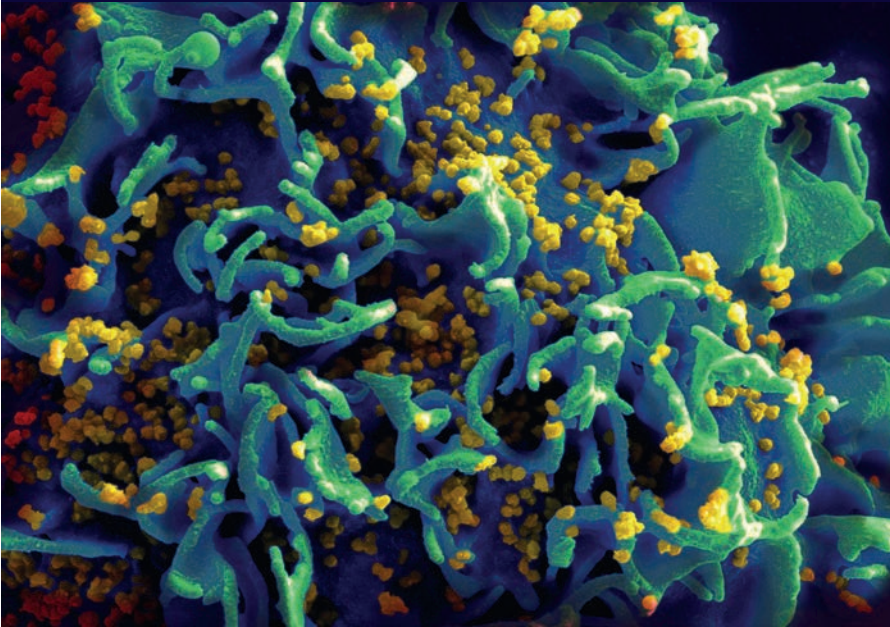


 MILESTONE 2

The discovery of HIV-1



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AIDS was first diagnosed in 1981 (MILESTONE 1) and, on the basis of epidemiological evidence, was soon speculated to be caused by an infectious agent. Around the same time, the first human retroviruses were discovered in T cells of leukemia patients and were associated with abnormal T cell replication. T cell function and numbers (MILESTONE 10, 13) are also affected in AIDS patients, and scientists hypothesized that a related retrovirus, preferentially infecting T cells, could be the infectious agent underlying AIDS.

Techniques developed during the work with animal and human retroviruses were essential to test this hypothesis and in isolating the putative retrovirus from AIDS patients. Scientists had already optimized in vitro culture conditions for long-term propagation of human T cells and relatively high retrovirus replication. They had developed sensitive techniques to detect reverse transcriptase, an enzyme essential and specific for retroviruses, and were able to identify retroviral particles by electron microscopy. Without this knowledge of retroviruses and essential techniques for their characterization, the discovery of HIV-1 would arguably have been much delayed.

In 1983, Luc Montagnier's team at the Pasteur Institute in Paris discovered HIV-1. Using the established techniques, they

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cultured T cells from a lymph node biopsy from a 33-year-old homosexual French patient with symptoms that can precede AIDS (subsequently called pre-AIDS), such as lymphadenopathy. Reverse transcriptase activity in the supernatant of this culture and the morphology of virions showed that they had isolated a retrovirus. They were able to infect T cells from a healthy donor, but attempts to infect other cell types, including B cells and fibroblasts, failed. The group concluded that this patient at risk for AIDS was infected with a T cell-tropic retrovirus, but an association with AIDS remained tentative at this point. In 2008, Luc Montagnier and Françoise Barré-Sinoussi from his team were awarded the Nobel Prize for the isolation and characterization of HIV-1.

In 1984, Robert Gallo's team at the National Cancer Institute in Bethesda,

Maryland, isolated HIV-1 from a larger group of patients and suggested causative involvement of the virus in AIDS. They isolated the virus from 48 individuals, including patients with symptoms of pre-AIDS and patients with AIDS, mothers of juveniles with AIDS and one healthy male homosexual. Overall, they isolated HIV-1 in approximately 47% of patients with pre-AIDS or AIDS, but in none of 115 heterosexual individuals with no known risk for AIDS. In the same year, Gallo's group made another important contribution to the field that allowed production of virus in higher quantities, facilitating further studies. After testing several human cell lines, they identified a T cell line that was permissive for HIV-1 and allowed long-term propagation of patient isolates.

A third team of scientists from the University of California, San Francisco, and the California Department of Health Services in Berkeley further strengthened the link between AIDS and HIV-1. Using similar techniques as the other groups, Levy et al. detected HIV-1 in 22 of 45 AIDS patients and antibodies to HIV-1 in 86 AIDS patients tested, as well as in a high percentage of homosexual men. Their isolates were antigenically and structurally related to the first isolate described by Montagnier's group.

In less than two years, at least three groups had isolated and characterized HIV-1, showing an association of HIV-1 with AIDS and suggesting a causal link. Each group initially gave the virus a different name, based on the symptoms of patients from whom the virus was isolated or on similarities to known viruses. At the time, HIV-1 was called lymphadenopathy-associated virus, human T cell leukemia virus type III and AIDS-associated retrovirus, in addition to other names. In 1986, a group of scientists suggested the name HIV-1, which is how we know the virus today.

Sonja Schmid,
Nature Communications

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