

UPDATE

National Cancer Institute/Office of Cancer Communications

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NEW LABORATORY RESEARCH ON HTLV-III VIRUS

National Cancer Institute scientists have found the first direct laboratory evidence the virus that causes acquired immune deficiency disease (AIDS), called HTLV-III, can by itself destroy the white blood cells that are the primary target of the disease.

Flossie Wong-Staal, Ph.D., an expert in molecular genetics who played a key role in the research, said, "The research indicates that the virus contains all the genetic information needed to destroy normal T4 white blood cells. It also definitively proves that the virus does not need interaction with other disease 'cofactors' to destroy these immune system cells."

Authors Amanda G. Fisher, Ph.D., Enrico Collalti, Ph.D., Lee Ratner, M.D., Robert C. Gallo, M.D., and Dr. Wong-Staal reported on their research findings in the July 18, 1985 issue of the scientific journal Nature.

They found that a complete DNA copy of the genetic information from the HTLV-III virus, when put into T4 white blood cells grown in the laboratory, makes viral proteins and complete virus particles that reproduce and infect the other T4 cells in the cultures. After 18 days, the virus begins to cause the death of the infected cells.

The experiment relied on an adaptation of a difficult laboratory technique called protoplast fusion. The technique, which fuses the internal components of a tiny bacteria with the contents of a human cell, is a type of transfection or mechanical introduction of foreign DNA into cells. In 1983, George H. Yoakum, Ph.D., and coworkers in Dr. Curtis Harris' NCI Laboratory of Human

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Last year, it was discovered by Drs. George Shaw and Beatrice Hahn of NCI, working with Drs. Wong-Staal and Gallo, that the surface of the AIDS virus is variable; it apparently can change as the virus is transmitted from one individual to another. The type of antibody found by the NCI scientists is called a neutralizing antibody because it binds to the virus and blocks attachment of the virus to cell surface receptors, thereby preventing it from infecting cells.

Neutralizing antibodies are specific for a precise site on the surface of a virus. That site must now be identified on the HTLV-III virus to determine whether the viruses isolated from a cross-section of people induce a common virus inactivating response. "We can use the laboratory test we developed to define the parts of the viral envelope that are important for stimulating the body to make the antibody," said Dr. Robert-Garoff. "Then we should be able to identify the specific genetic regions in the virus that are responsible for making that part of the surface."

Other scientific groups have looked for neutralizing antibody to the AIDS virus. In the same issue of Nature, Dr. Robin Weiss and his colleagues at the Institute for Cancer Research, Chester Beatty Laboratories in London, used a different laboratory approach to identify the existence of the antibody in AIDS patients. Last April, Dr. Martin Hirsch and colleagues at Massachusetts General Hospital in Boston also reported at the International Conference on AIDS in Atlanta that they had preliminary evidence for the existence of neutralizing antibody to the AIDS virus. The NCI and Weiss papers are the first definitive studies on the antibody that have been published in the scientific literature.

The NCI scientists developed the neutralizing antibody test by infecting H9 cells with the prototype HTLV-III, one of the several variants of the virus

isolated by Dr. Gallo's laboratory in 1984. H9 cells are the original white blood cell line that permitted the replication of HTLV-III without destroying the host cells, enabling scientists to isolate and mass produce the AIDS virus.

The scientists found that blood serum from a patient diagnosed with AIDS-related complex, a syndrome of abnormalities characterized by less severe immunological damage than AIDS, prevented the infection of cells by virus, thereby stopping the growth of the virus. They then showed that immunoglobulin, the complex blood protein of antibodies, was responsible for this activity, and demonstrated that the activity was specific for HTLV-III. They then analyzed blood samples from children and adults with AIDS, patients with AIDS-related complex, healthy homosexuals and heterosexuals, normal individuals at risk of developing AIDS, and patients with illnesses not related to AIDS.

The next phase of the research will be a blind study of blood samples of patients with varying stages of AIDS-related immune dysfunctions, to correlate more precisely the extent of disease with antibody levels.

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