DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
Building : 31
Room : 7A32
(301) 496- 5717

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Attention Writers and Editors:

The enclosed item describes research demonstrating that DNA viruses such as herpes simplex, chickenpox, and adenovirus, have the potential to stimulate latent AIDS viruses in cells. This stimulation would cause the AIDS virus to begin making more copies of itself, and has implications for understanding why some persons infected with the AIDS virus become sick within months while others remain healthy for years.

The research article, by Drs. Howard E. Gendelman, Senior Scientist, and Malcolm A. Martin, Chief; Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, NIH and their colleagues, appears in the second December 1986 issue of the Proceedings of the National Academy of Sciences, and is entitled "Trans-Activation of the Human Immunodeficiency Virus Long Terminal Repeat Sequence by DNA Viruses."

Please note that PNAS has embargoed release of information from this issue until Tuesday, December 30.

If you need additional information, please call me or Sandy Hecker, 301-496-5717.

Sincerely,

Patricia Randall

Patricia Randall
Chief, Office of Research Reporting
and Public Response
National Institute of Allergy and
Infectious Diseases

UPDATE

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

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Sandy Hecker
(301) 496-5717

ACTIVATION OF HIV BY DNA VIRUSES

New evidence shows that a wide range of DNA viruses have the capacity to stimulate latent AIDS viruses present in infected cells to produce additional viral particles. These particles could then infect other cells in the body. DNA virus stimulation of latent AIDS viruses may play an important role in determining which infected individuals will remain healthy, and which will develop the symptoms of AIDS.

Epidemiologic studies indicate that only about 20 to 30 percent of persons infected with the human immunodeficiency virus (HIV) develop AIDS within five years of infection. In the majority of infected individuals, HIV appears to be present in latent form--simply existing in the infected cell or producing such small amounts of additional HIV that the new viruses do not cause damage to the immune system leading to disease. However, other HIV-infected persons develop AIDS within months, or a year, of their initial infection with HIV. This different response to the virus makes some scientists think that HIV may require a stimulus or cofactor for its activation. Since most AIDS patients are also very susceptible to infection-causing microorganisms, scientists have speculated that such secondary infections might cause a dormant AIDS virus to become active (make more copies of itself).

To test this hypothesis, Drs. Howard E. Gendelman, Senior Scientist, and Malcolm A. Martin, Chief; Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), and their collaborators examined the effects of various human disease-causing DNA viruses on the portion of the HIV that regulates its infection of human cells. They tested DNA viruses (so-called because their genetic material is DNA) responsible for oral herpes (herpes simplex), respiratory infections (adenovirus), chickenpox and shingles (varicella-zoster), and degenerative neurological diseases (JC virus). To determine the effects of the DNA viruses, the researchers carried out experiments in which human cells growing in test tubes were exposed to the main regulatory element (called the long terminal repeat or LTR) of HIV along with one type of DNA virus. In each case tested, the control region of HIV was "turned on" by the added DNA virus.

Because the various DNA viruses that seem to activate HIV differ greatly in both their structure and function, the researchers think that the DNA viruses do not act directly on HIV but instead exert their effects through normal cellular intermediates. The scientists hypothesize that one or more normal cellular genes can be stimulated by a variety of factors, including DNA viruses, to make products which then

cause the HIV LTR to "switch on" and begin the process of making more copies of the AIDS virus.

This research is reported in the paper entitled, "Trans-Activation of the Human Immunodeficiency Virus Long Terminal Repeat Sequence by DNA Viruses," and is published in the Proceedings of the National Academy of Sciences, second issue for December 1986. The authors are Drs. Howard E. Gendelman (1), William Phelps (5), Lionel Feigenbaum (4), Jeffrey M. Ostrove (2), Akio Adachi (1), Peter M. Howley (5), George Khoury (4), Harold S. Ginsberg (3,6), and Malcolm A. Martin (1).

(Laboratories of (1) Molecular Microbiology, (2) Clinical Investigation, and (3) Infectious Diseases, NIAID, NIH, Bethesda, MD; Laboratories of (4) Molecular Virology and (5) Tumor Virus Biology, National Cancer Institute, NIH; and (6) College of Physicians and Surgeons, Columbia University, NY)