

HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

EMBARGOED UNTIL
6p.m., EST, Wednesday
April 9, 1986

PUBLIC HEALTH SERVICE
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Scientists at the National Institutes of Health have engineered a recombinant vaccinia virus that can be used as an important new tool in the study of acquired immunodeficiency syndrome (AIDS) and may have potential as a vaccine against the disease.

The recombinant virus produces the envelope proteins of the retrovirus, HTLV-III, that causes AIDS. Scientists anticipate that the new recombinant virus will be useful in studying how HTLV-III envelope proteins are made and what immune mechanisms might offer effective protection against the AIDS virus.

When injected into mice, the recombinant virus stimulates production of antibodies to the HTLV-III envelope proteins. Whether or not these antibodies can protect against infection with the AIDS virus is not yet known. The recombinant virus cannot cause HTLV-III infection of cells because only the envelope gene of the AIDS virus is included.

The study was reported in Nature (April 10, 1986) by Drs. Sekhar Chakrabarti and Bernard Moss from the National Institute of Allergy and Infectious Diseases, and Drs. Marjorie Robert-Guroff, Flossie Wong-Staal and Robert C. Gallo of the National Cancer

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Institute. The investigators used a technique developed in Dr. Moss's laboratory to turn the vaccinia virus, originally used as a vaccine against smallpox, into a vector to express genes from other microorganisms.

Using genetic engineering methods, Dr. Moss is able to construct new kinds of recombinant live virus vaccines by inserting bits of genetic material from other disease-causing agents into the vaccinia virus. The resulting hybrids retain the vaccinia virus' ability to produce local infection when inoculated in the skin of a wide variety of animals, thereby stimulating an immune response. In previous studies, Dr. Moss and his colleagues have immunized and protected experimental animals against several diseases, including hepatitis, herpes, influenza, and rabies.

In the study using HTLV-III, Dr. Moss and his colleagues inserted the envelope gene into the vaccinia virus vector. The gene is first expressed as a long precursor protein. With maturity, this protein splits into two glycoproteins: gp 120, which is required for the HTLV-III to attach to and infect cells; and gp 41, which anchors gp 120 in the virus membrane. Various tests confirmed that the HTLV-III gene in the recombinant virus synthesized both envelope proteins of the AIDS virus. Antigenicity was shown by the ability of the proteins to react with HTLV-III antibodies in immune sera.

The ability of the proteins to stimulate an immune response (immunogenicity) was tested by inoculating mice with purified recombinant virus. Sera from those mice and from control mice were incubated with proteins from HTLV-III-infected cells. The sera from

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mice that had been inoculated with the recombinant virus contained antibody that reacted with HTLV-III. Sera from the control mice did not react with the AIDS virus.

Using this recombinant technique, scientists may be able to genetically engineer alternate forms of envelope proteins, thereby pinpointing and even enhancing immunogenic HTLV-III proteins.

Dr. Anthony S. Fauci, director of the NIAID and coordinator of AIDS research at the NIH, pointed out that it is possible that the recombinant virus could be used directly as a live vaccine, or it could be used to infect cells in a tissue culture. The envelope proteins could be harvested from these cells and used as a subunit vaccine, which contains only part of the infectious organism.

Further study is needed to learn whether antibodies to the envelope proteins can reduce the infectivity of the AIDS virus and if vaccination that stimulates these antibodies might be protective. The envelope proteins are considered possible candidates for vaccine material since the corresponding proteins of mouse retroviruses can induce protective immunity against mouse leukemia. Variations in the structure of the envelope proteins from different HTLV-III isolates, however, is still a major concern.

Vaccines in general are designed to protect uninfected persons against disease. Scientists anticipate that an AIDS vaccine probably would not benefit persons already infected with HTLV-III.

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RECOMBINANT DNA TECHNOLOGY IN THE PRODUCTION OF AN AIDS VACCINE

