

# STATEMENT

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Office of Cancer Communications  
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## New Test for AIDS Virus Developed

Scientists at the National Cancer Institute's Frederick Cancer Research Facility (FCRF) have developed a new, rapid test for detecting and measuring the amount of the AIDS virus present in human cells growing in the laboratory. The virus that causes AIDS is called human immunodeficiency virus (HIV).

The test has the potential for use in finding drugs to treat AIDS.

It is not yet known if the test has the potential for routine use for testing individuals for HIV infection or for use in large-scale screening of the blood supply.

Barbara Felber and George Pavlakis of FCRF's Basic Research Program reported details of the new technology in the January 8, 1988, issue of Science.\* The Basic Research Program is operated by Bionetics Research, Inc., under contract with the National Cancer Institute (NCI).

The test is one of the first applications of genetic engineering techniques to detect HIV. It takes advantage of our current scientific knowledge about how the virus works after it infects human cells.

A major application of the test is rapid screening for new drugs against HIV. The test can be read in two days.

\*The paper is titled "A Trans-Activation-Based Bioassay for the Detection and Quantitation of HIV-I."

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The test can measure how well candidate AIDS drugs stop the virus from replicating. For example, the scientists were able to tell that the drug ddC (dideoxycytidine) is 50 times more effective than AZT (azidothymidine) in reducing HIV replication in the cells in tissue culture. AZT is the first AIDS drug found useful in treatment and is now commercially available for the majority of AIDS patients. ddC is currently in early patient testing as a possible new treatment.

In the future, the test also may provide physicians with an easier, less expensive, and more accurate way of monitoring patients' HIV levels than is now available. The test works both in human T cells that are killed by the virus and in other human cells like macrophages that can harbor the virus.

The new test uses human cells that have a gene for a bacterial "reporter" enzyme inserted into their DNA in such a way that when HIV infects the cells, they begin to produce a "reporter" enzyme. Very low levels of virus can be detected with the new test. In a typical test, as few as 10 virus-infected cells can be detected in the presence of one million cells.

When HIV infects cells, it produces proteins that stimulate the cells to produce large amounts of virus. One protein that is responsible for regulating this process is tat, the viral transactivation protein that boosts viral production. Tat stimulates protein production by interacting with other regulatory signals on the virus. These signals reside in a segment of the viral genetic information called the LTR, or long terminal repeat. LTR elements are a characteristic of the large family of viruses, called retroviruses, that includes HIV.

The FCRF scientists attached a bacterial "reporter" gene to the LTR of the AIDS virus, and inserted this recombined DNA stably into the genetic information (DNA) of human T cells or macrophages, two types of human immune

system cells susceptible to HIV infection. As a result, these cells were converted into indicator cells that respond to HIV infection by producing the bacterial enzyme, the "reporter" for the test. After two days, the scientists measure the levels of "reporter" enzyme which reflect the amount of HIV that is present. The test is specific for HIV and is not influenced by several other viruses.

The "reporter" enzyme is CAT (chloramphenicol acetyltransferase), a bacterial enzyme frequently used in recombinant DNA research. It was selected as a good "reporter" because it does not exist in human cells (so any that is detected is the result of HIV infection), is very stable, and can be measured easily and reliably. At present, CAT enzyme is measured automatically on ELISA plates by the intensity of color produced. ELISA is a technology commonly used in clinical laboratories for several different types of tests. The new technology can use other "reporter" enzymes as well. For example, by constructing indicator cells that contain the gene for luciferase, the protein that makes fireflies glow in the dark, the FCRF scientists hope to produce even more sensitive indicator cells.

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