

# UPDATE

National Cancer Institute/Office of Cancer Communications

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## NEUTRALIZING ANTIBODY TO HTLV-III VIRUS

Scientists at the National Cancer Institute and at the Chester Beatty Laboratories in London have detected a neutralizing antibody in some people who have been exposed to the virus that causes AIDS.

Although the number of people tested so far is small, the antibody levels in blood samples of patients appear to decrease with increasing severity of immune system impairment. The findings suggest that the antibodies may be protective.

"Knowing the antibody exists shows that our bodies are able to respond immunologically to the HTLV-III virus, which causes AIDS, in a way that may lead to new prevention and treatment approaches," said Dr. Marjorie Robert-Guroff, Ph.D., who coauthored a report on the new findings with Monica Brown, M.S., and Robert C. Gallo, M.D., of the NCI Laboratory of Tumor Cell Biology. "We can now study whether the antibody levels are naturally high enough in some people to provide protection from AIDS."

The research is published in the July 4, 1985, issue of the scientific journal Nature.

The scientists developed a laboratory test to detect the antibody. They will use the test to analyze possible vaccine preparations being developed against the virus.

"A key question now is whether the antibody is able to neutralize the infectivity of all isolates of the HTLV-III virus, the cause of AIDS, equally well," said Dr. Robert-Guroff.

(More)

Carcinogenesis modified the technique for research with human epithelial cells.

In Dr. Gallo's laboratory, one of the first to use the procedure with white blood cells, the scientists first inserted a complete DNA copy of the genetic information in the HTLV-III virus into a plasmid, which was put into a bacterium. The bacterium was then fused to normal human T cells grown in tissue culture.

"Using this technique, about 70 to 90 percent of white blood cells take up foreign DNA. However, only about one in 1,000-10,000 retain it," said lead author Dr. Amanda Fisher, a post-doctoral fellow from Great Britain who has been working with Dr. Wong-Staal and Dr. Gallo since 1983.

"We were able to show that, after transfection, the number of T-cells expressing virus increases from less than 0.1 to 15 percent within 13 days. We then verified that the DNA in the virus particles was the same as the DNA we transfected into the T-cells.

"The procedure demands extremely careful and precise laboratory techniques," cautioned Dr. Fisher. "Very few laboratories have reported the ability to do it successfully with human white blood cells."

When the NCI scientists then examined the cells for biochemical evidence that the HTLV-III virus was actively growing in the cultures, they found the viral enzyme (reverse transcriptase) and viral structural proteins in addition to the genetic information of the virus. Under the electron microscope, they were able to see complete virus particles.

By 31 days after transfection, the scientists could no longer detect the HTLV-III virus, and the number of T-cells in the cultures were greatly reduced.

The scientists now will be able to pinpoint the precise part of the viral genetic information that is responsible for the ability of the virus to kill

T4 cells. They are also studying how the virus causes destruction of the entire population of normal T4 cells in the laboratory cultures, even though only a small proportion of the cells in the experiments showed evidence of biologically active HTLV-III virus after transfection.

Recently, Dr. Wong-Staal and other scientists in Dr. Gallo's laboratory reported on related research to examine how the HTLV-III virus works inside human cells. In particular, they are interested in determining whether the virus acts by regulating the expression of specific cellular genes.

This type of genetic regulation was proposed in 1984 by Dr. William Haseltine and coworkers at the Harvard Medical School to explain the ability of the HTLV-I and II viruses, known human cancer viruses, to cause cancer-like changes in laboratory cultures of human cells.

In two papers published in the June 28 issue of the scientific journal Science, groups of scientists at the National Cancer Institute, led by Dr. Wong-Staal, and at Harvard Medical School, led by Dr. Haseltine (in collaboration with Dr. Wong-Staal), reported discovery of a previously unidentified gene in the HTLV-III virus. The reports said the gene may be controlling the rate at which human cells make the HTLV-III virus. The more virus an infected cell makes, the more rapidly the virus can spread to other cells.

The structure of the predicted protein made by this tiny gene is consistent with that of other nuclear proteins that bind to nuclear DNA, and possibly to genes that regulate cellular growth functions.

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