



Update

FOR RELEASE
Wednesday, June 15, 1988

PUBLIC HEALTH SERVICE
Laurie K. Doepel
(301) 496-5717

TUMOR NECROSIS FACTOR INDUCES HIV FROM A CHRONICALLY INFECTED T-CELL CLONE

Scientists have discovered that a key chemical messenger of the immune system, tumor necrosis factor (TNF), can activate human immunodeficiency virus (HIV) lying dormant inside T cells. Because TNF helps regulate the normal immune response, this finding may have important implications for understanding how HIV infection evolves into AIDS.

Results of this study--conducted by Dr. Thomas M. Folks of the National Institute of Allergy and Infectious Diseases (NIAID), Dr. Kathleen Clouse of Georgetown University, and NIAID scientists Mr. Jesse Justement, Dr. John H. Kehrl, and Dr. Anthony S. Fauci--were presented by Dr. Clouse at the Fourth International Conference on AIDS in Stockholm.

TNF is one of multiple monokines, chemical messengers produced by scavenger cells of the immune system known as monocytes and macrophages. Although it was initially discovered about 15 years ago because of its cancer-killing activity, it has since been found that immune system cells produce this important molecule during a wide range of active infections and also employ it to help maintain normal immunoregulation.

Because of these latter two functions, the researchers theorize that TNF could accelerate the progression of AIDS once opportunistic infections appear but may also contribute importantly to disease development earlier in HIV infection.

In their study, the scientists tested several recombinant (laboratory-made) monokines for their ability to activate HIV. They wanted to see if monokines can induce HIV expression in a chronically HIV-infected T-cell line, that is, a clone of T cells in which HIV genes are

integrated into the DNA of the cells but are not actively producing virus. Those monokines tested included recombinant forms of TNF-alpha and -beta, interferon-gamma, four interleukins, and platelet-derived growth factor. Only the two forms of recombinant TNF (rTNF) caused substantial HIV activation. Furthermore, these effects occurred at far lower concentrations than expected, according to the scientists. rTNF-alpha's effects were seen at the level of a trillionth of a gram, and rTNF-beta's at the level of a billionth of a gram.

The springboard for the work reported here was another recent study conducted by Dr. Clouse, Dr. Folks, Dr. Fauci, and Drs. William Farrar and Paul Barstad of the National Cancer Institute. In that study they found that incubating the T-cell clone with a "soup" of monokines (one of which is TNF) derived from artificially stimulated monocytes drives out infectious HIV from these cells.

The chronically infected T-cell clone used in these experiments was developed by NIAID scientists Mr. Douglas Powell and Dr. Folks. With this model system, scientists can now study monokine regulation of HIV expression in T cells. This is important because T4 cells, a subset of T cells, are the main immune system cell targeted by HIV, and monokines are part of the complex language of chemical signals that orchestrate the body's defensive reactions.

"These findings with tumor necrosis factor," commented Dr. Folks, "provide new evidence that by-products of the normal immune response can control HIV replication and may play a major role in the progression of HIV infection."

#