



National Institute of Allergy and Infectious Diseases

Update

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PUBLIC HEALTH SERVICE
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NEW AIDS VIRUS GENE DISCOVERED

National Institute of Allergy and Infectious Diseases (NIAID) visiting associate Dr. Klaus Strebel has identified a ninth gene of the human immunodeficiency virus (HIV, the cause of AIDS). He and his colleagues have found evidence that the protein specified by the new gene, called "U," may be involved in the assembly of viral particles. Discovery of this new gene is enabling scientists to decipher and better understand HIV biological processes such as its ability to persist in the body. Such understanding is ammunition in the battle against AIDS.

The U gene lies between the HIV "tat" and "envelope" genes on the map of the HIV genome and codes for production of a 16 kilodalton protein made up of 81 amino acids (protein subunits). Antibodies (protective proteins produced by the immune system) against the U protein were detected in blood samples from 5 of 15 persons with AIDS showing that the protein is synthesized during HIV infection of humans.

Dr. Strebel, NIAID Laboratory of Molecular Microbiology (LMM), Dr. Thomas Klimkait, guest researcher, LMM; and Dr. Malcolm A. Martin, chief, LMM have characterized the U gene and protein. Comparison of the U gene genetic sequence among all published Zairian and North American HIV isolate sequences revealed that regions of the gene are remarkably similar suggesting that the protein plays an important role in HIV infection.

When the researchers purposely mutated (changed) the gene's genetic information in the

laboratory, resulting viral particles appeared abnormal when observed through an electron microscope. In addition, cells that contained HIV with mutated U genes appeared to release four to ten times fewer viral particles than those containing wild-type HIV (those with an intact U gene). The released particles, however, showed no difference in their ability to kill cells. At the same time, about five times more viral proteins were detected inside cells infected with mutant U-containing HIV, than were seen in cells infected with wild-type HIV. These and other experimental results indicated to the scientists that the U protein is involved in HIV particle maturation.

The research team is continuing studies of the U protein to elucidate its role in HIV infection. A number of viral isolates recovered from HIV infected individuals contain natural mutations affecting the U gene. Since mutations slow the production of viral particles, one possibility may be that the U protein is involved in HIV persistence--the ability of HIV to infect humans for long periods of time--for example, more than five years.

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