



Update

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HIV: New Findings

Dr. Anthony S. Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID) and Chief of the NIAID Laboratory of Immunoregulation (LIR), today reported on the ability of the human immunodeficiency virus (HIV), the cause of AIDS, to infect bone marrow cells. He also described a molecular mechanism by which latent HIV infection is converted to active infection. Dr. Fauci mentioned these new findings during delivery of the honorary George M. Kober Lecture on May 2 at the joint plenary session of the Association of American Physicians, American Society for Clinical Investigation, and the American Federation for Clinical Research meeting in Washington this week.

A wide range of blood-related abnormalities exist in persons with AIDS. This fact, together with the often low level of detectable HIV in circulating blood cells, suggested to researchers that bone marrow cells--the progenitors of the types of cells that make up blood--may be infectible with and harbor HIV. Scientists already know that macrophages, an important immune system cell, can actively produce and harbor HIV without being killed, unlike T4 cells, which are killed when HIV is actively produced in them.

Dr. Thomas Folks, a senior investigator in LIR, Dr. Stephen Kessler, of the Uniformed Services University of the Health Sciences, in Bethesda, Maryland, Dr. Fauci and others have now shown that HIV can infect certain bone marrow cells. These infectible cells have characteristics of myelomonocytic cells that may develop into monocytes--immune system cells that can develop into macrophages. Dr. Fauci and his colleagues found that HIV can propagate and remain within these bone marrow cells. Thus, these cells may be additional

reservoirs of HIV.

To do the experiments that provided these results, the research team developed a new technique to separate these specific cells from other types found in the bone marrow. Prior to development of this procedure, such separation had been extremely difficult to do and was prone to contamination with other cell types, which would bias research results.

Dr. Fauci and his colleagues are also characterizing factors that may convert a latent infection to a productive infection. One of the most important AIDS-related questions is "what stimulates latent HIV infection to active infection?" The Centers for Disease Control estimate that 1.5 to 2 million Americans are currently infected with HIV. Most of these people have no clinical symptoms.

Most recently, Drs. Folks, Fauci, and others have demonstrated how certain cytokines (cellular hormones) stimulate latent infections to active infections. Their experiments indicate that cytokines act on the switch-like long terminal repeat (LTR) region of HIV's genetic material. When the LTR is switched off, no progeny (offspring) viral particles are made. The researchers demonstrated in laboratory tests with human HIV-infected T4 cells that cytokines can switch on the LTR. Some cytokines are present at high levels in persons who are infected with microorganisms such as viruses and parasites. Activation of HIV by cytokines may explain in part why concurrent infections with other viruses seems to stimulate progressive HIV infection.

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