

# COLUMBIA SPECTATOR

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## AIDS researchers' t-cell work brings hope

By Gail Javitt

Researchers at Columbia's College of Physicians and Surgeons (P&S) made a discovery last year that has been key to the understanding of how the AIDS virus enter the cells of the body.

T cells, white blood cells in the body responsible for initiating an immune response, are a vital part of the mechanism by which the AIDS virus enters the cells, P&S researchers learned last year.

According to Higgins Professor of Biochemistry and Microbiology Dr. Richard Axel, who identified the mechanism, the AIDS virus binds to a protein on the surface of a type of T cell. Once the virus is bound to this protein, called T4, it can enter and take over the cell for its own use. By using the cell's own DNA and proteins, the AIDS virus can multiply and kill the cell.

Axel said the role that the T4 protein plays when it binds to the AIDS virus is not its normal function in the cell. T4 exists on T cells called "helper cells." The job of helper cells is to activate "killer cells" so that they can kill foreign particles that enter the



body. T4 allows helper cells to carry out their role by bringing them near these disease-bearing particles.

Ordinarily, when T4 brings the helper cells near the foreign particle it does not bind to the particle, Axel said. What is unique about the AIDS virus is that it is the only virus to which T4 attaches itself.

"The association [of T4] with the AIDS virus is exceedingly tight," Axel said.

Without this association, the virus could not enter the cell. According to Axel, only those parts of the body whose cells have T4 are infected with the AIDS virus. These organs include the brain, the blood and the spleen.

According to Axel, "anything that blocks the interaction of T4 with the viral coat of AIDS will stop viral infection."

Axel said that recent efforts to synthesize a compound to block the association of T4 with the AIDS virus is showing promise. A compound like this "may be an effective therapeutic," or drug, Axel said.

Axel's work does not focus on the AIDS virus itself. He said it was when he was working on research unrelated to AIDS that he identified the T4 protein.

"[I] came to this [discovery] through an interest in cell intimacy," meaning how cells in the body interact with one another, Axel said.

But Axel is not the only P&S researcher who is studying the relationship between T cells and the AIDS virus. According to Professor of Medicine Dr. Leonard Chess, who collaborated in the identification of T4, T cells may also be the site at which the AIDS virus lingers during the interim period between infection and attack on the cells of the body. Moreover, as



soon as the virus does become activated, it attacks and takes over the T cell, which prevents the T cell from initiating an immune response.

Chess said that the T cells themselves may be activating the virus, to their detriment and the detriment of the body. Laboratory experiments have shown that the virus grows much better in a T cell that is activated to perform its normal immune function than in a T cell that is inactive.

“The very process that is normally used to get rid of the virus may be what activates this virus,” Chess said. Normally, T cells are activated and attack a virus, but with AIDS, activated T cells are themselves attacked by the virus.

Related types of white blood cells that have become important in studying the virus are macrophages. According to Chair of the Department of Physiology and Cellular Biophysics Dr. Samuel Silverstein, who studies macrophages, they are also “an important reservoir of AIDS virus in man.” Macrophages are “phagocytic,” which means that they are scavengers that roam the body eating debris such as dead cells.

“[Without macrophages], your insides would look like the streets of New York,” Silverstein explained.

Macrophages also “defend against pathogenic microorganisms,” such as tuberculosis, Silverstein said. They work by inhibiting the growth of pathogens, or disease producing agents, when they are activated by a certain hormone. Silverstein said that one



reason AIDS patients are subject to "opportunistic infections" like cancer is because not enough of this activating hormone is being produced.

According to Chess, a key question to ask about immunity is what kind of immune response is made against the AIDS virus.

Most viruses are destroyed by proteins in the blood that recognize and remove foreign particles from the body. However, if these proteins, or antibodies, do not play a role in the immune response to AIDS, then the usual man-made vaccines will not be effective, because vaccines work by stimulating the body to make antibodies.

According to Higgins Professor of Microbiology and Medicine Harold Ginsberg, "Our knowledge is such right now that we really don't know whether the classical way of immunization will [be effective]."

Ginsberg explained that, at present, vaccines are only effective against "free" viruses, in which case they prevent the virus from infecting the body. However, if a virus is not free, but is, rather, transmitted inside a cell, then there are no vaccines that will work. Ginsberg said that it is not known whether AIDS is a free or intracellular virus.

Ginsberg said that he hopes that the research presently being done at P&S will lead to the development of vaccines against the AIDS virus.

## **AIDS RESEARCH AT COLUMBIA**

**Last in a series**