Do HIV-infected blobs run amok in AIDS?

Wreaking destruction as it crawls, a massive amoebalike creature envelops each living thing that it lures close. The creature finally explodes, showering the area around it with deadly viruses that create replicas of the original monster.

A script for a bad horror movie, perhaps a sequel to *The Blob*? Nope, it's just a new take on how the AIDS virus, HIV, might work within the body.

When researchers infect human immune cells with HIV in laboratory dishes, they often observe the infected cells fusing into massive entities known as syncytia. Most AIDS scientists consider syncytia a laboratory phenomenon with little relevance to the disease, but David R. Soll of the University of Iowa in Iowa City contends that the multicellular masses occur within HIV-infected people.

He also argues that syncytia may explain some of the ravages of AIDS, even accounting, at least in part, for the immune system decline seen in people infected with HIV. "You cannot avoid syncytia anymore. They just have too many capabilities. They're motile, destructive, invasive, infectious, and seductive," says Soll.

In 1996, Sarah S. Frankel of the Armed Forces Institute of Pathology in Washington, D.C., and her colleagues refocused attention on syncytia when they reported that 11 out of 13 people with HIV had virus-containing syncytia in their adenoid tissue. At this week's American Society for Cell Biology meeting in San Francisco, Soll and his colleagues presented evidence that similar syncytia are found in samples of lymph nodes and blood taken from HIV-infected people. Frankel says that her group has also recently found HIV-induced syncytia in tissues other than adenoid, albeit not in lymph nodes.

Using devices designed to visualize moving cells, Soll's group has even observed syncytia crawling out of some samples of lymph node tissue as if a syncytium were a single cell. Syncytia, which can consist of thousands of cells fused together, crawl by extending a footlike growth that may be as large as a hundred cells.

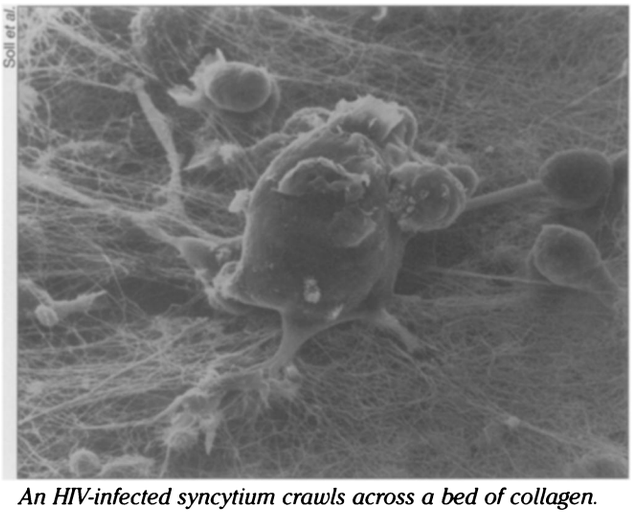
In laboratory experiments by Soll's group, mobile syncytia disrupted membranes made from collagen, a major structural protein in lymph nodes, and punched holes in endothelial tissue, which lines blood vessels. These destructive tendencies, says Soll, may help explain why people with AIDS often have leaky blood vessels and lymph nodes that appear torn apart.

In the lab dishes, HIV-induced syncytia rarely live more than several days. Because syncytia induced by a chemical treatment survive much longer, Soll concludes that the death of the viral syncytia most likely stems from the massive replication of HIV within them.

"Syncytia are short-lived, but they're self-perpetuating. Every time one blows up, so much virus comes out of it that everything around it gets infected and starts fusing," he notes.

Syncytia may also act as sirens, luring immune cells to their doom. A syncytium secretes at least two proteins that attract immune cells to fuse with it. One is an HIV protein called gp120. The second has been identified, says Soll, but his university's lawyers won't allow its disclosure until they file patents. Theoretically, drugs that inhibit the syncytia's attractants might slow the immune system decline that occurs in AIDS, he says.

Other AIDS researchers note that syncytia were a hot topic when HIV was discovered 15 years ago, but a consensus emerged, and still holds, that they are a rarity in the human body. "Convincing people that they're there in abundance is likely to be a mini-war," says Robert C. Gallo of the Institute of Human Virology in Baltimore. —*J. Travis*



An HIV-infected syncytium crawls across a bed of collagen.

Tumors often have phony protein receptor

When a cell becomes infected or severely damaged, it normally receives a signal to commit suicide. One self-destruct button, a protein called Fas or Fas receptor, sits on the surface of most cells in the body. The thumb on the Fas button is Fas ligand. Once bound together, the two proteins instigate a chain of events called apoptosis that leads to the cell's orderly breakup.

Sadly, in cancer cells, this cascade of events doesn't always start on cue. A new study suggests that tumor cells can outwit the immune system by making large quantities of a phony, ineffective version of Fas.

The immune system, which is geared to fight foreign invaders, doesn't routinely wipe out tumors because it considers them to be part of the body. Some immune system cells, however, do recognize cancer cells as abnormal and therefore as candidates for apoptosis. Even then, when these immune cells arrive to instigate the suicide program, their Fas ligand doesn't work on some cancer cells.

According to the recent study, the phony version of Fas receptors on the cancer cells binds with Fas ligand, preventing it from hooking up with real Fas receptors and from starting the apoptosis cascade, researchers report in the Dec. 17 NATURE.

Cancerous cells whose genes direct production of plenty of the decoy receptor may survive and replicate, while other cancer cells are removed by the immune system via apoptosis, says study coauthor Avi Ashkenazi of Genentech in South San Francisco, Calif.

"If that's true, and that's a big 'if,' then it suggests that a tumor has the ability to keep ahead of the immune system," says Alan N. Houghton, an immunologist at Memorial Sloan-Kettering Cancer Center in New York City.

Using tissue from 23 cancer patients, Ashkenazi and his colleagues found that many tumors produced the decoy Fas but surrounding healthy tissue did not. They detected the decoy in 6 of 15 lung tumors, in 2 of 5 breast tumors, in both colon tumors examined, and in the single stomach tumor studied.

In another experiment, extra copies of the gene that encodes this decoy protein showed up in 17 of 35 lung and colon tumor samples. Noncancerous tissue samples contained no extra copies, Ashkenazi and his colleagues report.

"I found this a very exciting paper," says Douglas R. Green, a cell biologist at the La Jolla Institute for Allergy and Immunology in San Diego. The study hints that Fas and Fas ligand may play a role that is fundamental to tumor growth, he says. Perhaps for a cell to become cancerous, it needs to both activate a proliferative mechanism "and come up with a way to avoid Fas, Fas ligand, and apoptosis," he says.

Synthetic antibodies that neutralize the decoy receptor might, if given as a drug, help the immune system attack many tumors, Ashkenazi says.

The decoy itself may also prove useful in medicine. Autoimmune reactions, in which the immune system attacks cells of the body, might be shut off by doses of the decoy version of Fas, says Noel R. Rose of Johns Hopkins Medical Institutions in Baltimore. —*N. Seppa*