Killer Cells, MHC: Factors in AIDS?

Squads of "killer" cells produced by the body are capable of destroying other cells infected with AIDS-causing viruses, two research groups reported this week. The findings may mean a better understanding of both AIDS vaccine development and why some infected persons develop full-blown AIDS while others do not.

However, the specialized cells may or may not be good news in terms of preventing the fatal disease. In those patients who develop AIDS, the complicated killing process — which involves genes that also govern the body's compatibility with transplanted tissues — may be a case of "too little, too late," or even of the body's own defense system doing more harm than good, suggest the scientists.

Using radioactive assays to measure the number of cells killed, scientists in France and the United States discovered that some of the blood cells called T lymphocytes turn into killers when confronted with other cells infected with the AIDS virus (HIV). The surfaces of those infected cells carry HIV material, which is recognized by the soon-to-be killer lymphocytes, whose presence had been noted in other viral diseases.

Mere one-on-one recognition, however, isn't enough for these killer cells, which require a "third party," called major histocompatibility complex (MHC), to handle the introductions. Scientists have known for several years that the target cell's surface also must hold materials coded for by a group of MHC genes. Unique to each individual, the MHC is responsible for the body's response to "foreign" tissue transplants and is related to some autoimmune diseases.

Both groups conclude in the July 23 NATURE that HIV-infected cells attract killer cells in a process controlled by an MHC component, the first time the mechanism has been described in AIDS. The French scientists did experiments more closely related to AIDS patients, while the U.S. team used a system that is part of the current push for an AIDS vaccine.

Researchers at Massachusetts General Hospital in Boston and the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Md., made target cells by collecting non-T lymphocytes from eight men who tested positive for the antibody to HIV and from five controls who tested negative. After being infected with recombinant vaccinia viruses containing different HIV genes, target cells from each donor were mixed with T cells either from that same donor (autologous) or from others (heterologous). None of the cells from negative subjects showed any killer-T activity, report the authors.

But in samples from positive individuals, there was a 2- to 14-fold increase in cell killing, with greater levels seen when the envelope-coding HIV gene was inserted into the vaccinia virus. Scientists developing AIDS vaccines are particularly interested in the HIV envelope as a noninfectious component that might induce immunity (SN: 5/9/87, p.297). The U.S. group reports that killing also was greatest when autologous killer cells were used, and responses using heterologous cells apparently occurred only when the two sets of cells shared MHC regions.

The French scientists, from the Institut Pasteur and two hospitals in Paris, took their studies a step closer to the clinic by using cells that had been washed from the lungs of positive patients with an AIDS-related respiratory disease. They found that killer T cells also interact with another white blood cell type called macrophages — which ingest HIV and, like lymphocytes, play a role in cell-mediated immunity. Although the antibody response to HIV has been fairly well described, the cellular response to the virus thus far remains largely a mystery.

Massachusetts General's Bruce D. Walker told SCIENCE NEWS that, while killer cells are important in recovery from certain viral infections such as influenza, their effect in AIDS is unclear. "We would think that their presence may be protective to some extent," he says. "But clearly [the killer response] doesn't seem sufficient [for the estimated 10 percent to over 50 percent of patients who go on to develop AIDS]."

The French scientists say that "the question remains as to the beneficial or deleterious effect of HIV-specific [killer-cell] activities in positive patients." They suggest that the interaction between the infected macrophages and the killer lymphocytes may exacerbate a patient's condition by causing inflammation that exposes the lungs, brain and other organs to further infection by bacteria or fungi associated with AIDS fatalities.

In addition, the Paris researchers say that when heterologous killing occurred, the cells from the two different AIDS patients shared specific MHC components called HLA-A2. Although a person's MHC is an inherited trait, NIAID's Thomas J. Kindt—who did not participate in the reported research — says it is far too early to say whether HLA-A2 individuals may be more susceptible to AIDS. He adds that, although there are examples of increased susceptibility to disease with certain HLA profiles, "unfortunately, there is no sweeping statement to be made about the genetic component of AIDS." *— D. D. Edwards*

Autoimmunity may cause infertility

The miracle of biological conception has long baffled geneticists, developmental biologists and just about everyone else who has taken a moment to think about it. But pity the immunologists who are stuck with the task of explaining how it is that a fertilized egg—which includes, after all, a fair share of father-furnished foreign material — manages to keep from being immunologically rejected by the mother.

That ultimate immunological question has yet to be answered (SN: 10/11/86, p.234), but scientists are making progress in understanding the many links between the fields of immunology and reproductive biology. Laboratory studies have already shown, for example, that antisperm antibodies in women can interfere with sperm function and fertilization — although little is known about where these antibodies come from or why some women appear to be more immunologically reactive than others.

Now researchers at Mount Sinai Medical Center in Chicago are using immunoreproductive studies to better understand the causes of infertility, and to provide clues about the body's business of self-recognition. Norbert Gleicher and his colleagues found that *in vitro-* ("test-tube-") fertilized women with abnormally high levels of autoantibodies (antibodies that erroneously attack normal tissue) got pregnant at only one-fifth the rate of women with normal autoantibody levels. Their research is to be published in the August OBSTETRICS AND GYNECOLOGY.

The study is the first to compare autoantibody levels in the blood with those in the follicular fluid — the fluid that bathes the fertilized egg near the ovaries — and hints at the possibility that the ovaries may be responsible for local production of autoantibodies.

"We found that women with abnormal autoantibodies in blood also have abnormal autoantibodies in follicular fluid," Gleicher told SCIENCE NEWS. "But what is even more important is that one group of autoantibodies, the phospholipids, appears to be concentrated in the follicular fluid in autoantibody-positive patients."

Gleicher kept track of *in vitro* fertilization successes in patients with and with-