Leukemic cells rehabilitated in rats

The odds that an individual will survive a bout with leukemia depend not only on the strength of that person's immune response, but also on his or her supply of a little-understood class of biological substances called differentiation factors, new research suggests. It is believed that one anticancer drug now in clinical trials—called granulocyte colony stimulating factor—may be a member of this mysterious class of substances, but nobody is really sure how many of these factors exist or how they work. Indeed, until now, all that's been known is that there is *something* in the extracts of certain mammalian organs that has the ability to induce differentiation (normal maturation) in cultured leukemic cells.

The new work is the first to quantify the effects of these factors on leukemia cells in living rats, and suggests that they may be more important as cancer-protective factors than researchers in the field previously believed.

The research, which appears in the Nov. 27 SCIENCE, was performed by Joaquin J. Jimenez and Adel A. Yunis of the University of Miami School of Medicine. They worked with myeloid leukemia cells, which are white blood cells that have failed to differentiate into their mature forms and that continue to proliferate indefinitely.

"Lots of people have shown that you can induce differentiation of cells *in vitro*" with the addition of a differentiation factor, Yunis says. "Our research attempts to answer one question: If you can push a leukemic cell to differentiate in the test tube, what then keeps it in a constantly self-renewing, undifferentiated state" in animals or patients with leukemia? The answer, he says, may be that leukemic patients are unable to generate by themselves appropriate amounts of that differentiation factor.

To test this hypothesis, Jimenez and Yunis extracted quantities of the factor from a variety of rat organs and performed experiments on test tube cultures of leukemic cells. They found that the more differentiation factor they added to the cells, the greater the number of leukemic cells could be induced to differentiate into normal, adult white cells. In similar experiments using live animals, the researchers found that rats given higher doses of differentiation factor were better able to survive injections of leukemic cells.

But because scientists still do not know the molecular structure of differentiation factor and can only deduce its presence in extracts by its action on cells, it was important to show that the rats' increased survival was due to an induced, normal differentiation of their leukemic cells and not to an immune factor that simply killed the leukemic cells. To find out, the researchers implanted into rats tiny screened cages, or diffusion chambers, containing a known number of leukemia cells. Cells could not enter or leave the chambers, but were bathed in the rats' body fluids—including various concentrations of injected differentiation factor.

After 48 hours, they retrieved the chambers and examined the cells. In rats with higher levels of circulating differentiation factor, 90 percent of the cells were still alive and 94 percent of them had differentiated. The rampant replication characteristic of leukemic cells had stopped. In control rats with no differentiation factor added, none of the trapped cells differentiated and cell proliferation continued unchecked.

The next steps are to purify, identify and try to mass-produce the factor or factors responsible for this differentiating activity, Yunis says. "As we get closer to purifying these factors, we should be able to get answers about how they work," he says.

"But whatever the mechanism is, and whatever these factors are, the experiment tells us that you can push these leukemic cells to differentiate *in vivo*. It indicates that the use of [supplemental] differentiation factor has potential therapeutic application." —*R. Weiss*

Second AIDS vaccine approved for testing

A second potential AIDS vaccine was approved last week by federal officials for human testing in the United States.

The vaccine was developed by Seattle-based Oncogen, a division of the Bristol-Myers Co. It will be given to 30 healthy homosexual males beginning in January at Seattle's Pacific Medical Center, according to study coinvestigator Ann Collier of the University of Washington School of Medicine. Another group of 30 controls will be involved in this phase of the study, which will examine the vaccine's safety and how it might influence the immune response.

Testing of the first potential AIDS vaccine, developed by MicroGeneSys, Inc., of West Haven, Conn., was approved by the Food and Drug Administration (FDA) last summer (SN: 8/22/87, p.116). Inoculation of human volunteers, who are predominantly homosexual males, began in September at the National Institute of Allergy and Infectious Diseases in Bethesda, Md. The only side effect so far has been redness near the inoculation site, which is typical for inoculations, says MicroGeneSys President Frank Volvovitz.

Both vaccines will expose volunteers to similar viral proteins found in the "envelope" structure surrounding the human immunodeficiency virus (HIV), which can lead to fully developed AIDS. The proteins will not cause HIV infection, researchers say, but should stimulate an effective immune response that protects against future HIV infection.

The vaccines will introduce viral proteins differently to the body. The Bristol-Myers experimental vaccine, called HIVAC-1e, is made from the vaccinia virus, which has been used to manufacture the smallpox vaccine. In the case of the potential AIDS vaccine, researchers have altered the vaccinia virus by inserting a gene coding for the HIV viral protein gp120. The hope is that after the vaccine enters the body, the gene will use the machinery of invaded cells to make gp120 proteins, which will then appear on the cell surface and be recognized by the body's immune system.

To make the MicroGeneSys vaccine, researchers inserted a gene coding for gp160 into a virus that infects moths and butterflies, placed the virus into cultures containing insect cells and produced a large quantity of the viral protein, which is used as the vaccine.

The studies of these and other vaccines will determine which triggers the best immune response, says Gerald Quinnan, director of the FDA's division of virology. In the "insect" approach, the protein will be floating freely in tissue fluids, while in the vaccinia approach, it will be on cell surfaces.

If the vaccines' safety and immune response are established, their ability to prevent HIV infection will then be studied.
—*S. Eisenberg*

Keeping topsoil down on the farm

Amid the steeply rolling hills of the Palouse region near Spokane, Wash., lies the ideal "laboratory" for testing the effects of different farming techniques on soil. In that area, one farm has relied on crop rotations and native soil fertility for plant nutrients ever since it was first plowed in 1909. Next to it, another farm, first cultivated in 1908, has been receiving recommended doses of inorganic fertilizers and pesticides since 1948. By examining the soil in two adjacent fields, one belonging to each farm, researchers have now been able to ascertain that an organic farming system is significantly more effective in reducing soil erosion than a system based on the use of manufactured fertilizers.

"The differences are dramatic," says John P. Reganold of Washington State University in Pullman. "People say there should be differences, but until now, no one had clear evidence." Reganold and his colleagues report their findings in the Nov. 26 NATURE.

The organic farm used in the study