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

operates on a three-year cycle. It produces winter wheat the first year, then a crop of spring pea the following year. Both crops are harvested. In the third year, Austrian winter pea is planted. The mature plants are plowed under to provide "green manure" for the fields. In contrast, the conventional farm alternates between crops of winter wheat and spring pea. Although the crop yields are similar for both farming systems, the organic farm produces a cash crop on a given field in only two out of three years of the cycle.

It took a long time to find the right sites for a comparison of soil properties, says Reganold. "We picked a spot where the farms touch each other." Even the slopes and the direction in which the slopes face were identical for both sets of test sites. "In that small area, all environmental conditions were the same except for management," he says.

Earlier studies had already shown that the organically farmed soil had higher levels of organic matter and a larger mass of microorganisms and soil enzymes. The most dramatic difference revealed by the new study was that the organic farm's topsoil was on the average 6 inches thicker than its neighbor's. In addition, the organically farmed soil held more moisture and had a softer surface crust. Says Reganold, "All that change has taken place since 1948."

The greater erosion rate shown for conventionally farmed soil indicates that a typical farm with similar soil and slopes could lose all of its topsoil within 50 years, exposing a denser, less fertile, clay subsoil. Wheat yields go down substantially in this harder soil.

If conventional farming systems are not modified, the loss of valuable topsoil will continue, and in the long term, productivity will decline, says Reganold. Unfortunately, many farmers can't afford to put in a legume-based, green-manure crop and periodically leave fields out of production. *– I. Peterson*

Tense moments between two quakes

Two earthquakes and a swarm of aftershocks struck California's Imperial Valley last week in a bout of crustal rearrangements that caused some scientists to worry that the so-called "big one" might follow on the heels of these smaller quakes. And this week, a quake registering at least 7.4 on the Richter scale of magnitude occurred in the Gulf of Alaska.

The larger of the California quakes, measuring 6.3 on the Richter scale, was centered on the Superstition Hills fault about 90 miles east of San Diego. The first earthquake, a 6.0 in magnitude, hit 11 hours earlier and 6 miles to the east, along an unnamed fault that trends northeast from the Salton Sea toward the southern branch of the San Andreas fault.

Scientists believe that the first quake triggered the second one. While this pattern is unusual, it is not unprecedented in the Imperial Valley.

These and most other earthquakes in the region result from the movement of two great crustal blocks that slowly slip past one another. As the northwest-moving Pacific plate slides against the North American plate, this motion is absorbed by the intricate faults in California and off its coast. Most of the strain from this plate motion is stored in the well-known San Andreas fault.

Though the earthquakes occurred on faults that lie 20 miles west of the San Andreas, scientists who monitored the aftershocks of the first quake became concerned when the cluster of temblors began to head toward the San Andreas. "We were definitely worried about the possibility of it going north and we were keeping a very close watch," says Lucile Jones, a seismologist with the U.S. Geological Survey (USGS) in Pasadena.

By all estimates the southern section of the San Andreas fault is just waiting to break. Instead of sliding peacefully past one another, the two sides of the fault have spent 300 years locked together, storing up the potential energy equivalent to a magnitude 8 earthquake. Seismologists estimate a 50 percent probability that the fault will break in the next 20 years.

While Jones and others watched the aftershocks to see if they would unlock the San Andreas, the northeast-moving aftershocks turned around and headed back toward the southwest. "Then the [magnitude] 6.3 [earthquake] occurred on the Superstition Hills, and we had aftershocks in the Superstition Hills, and we sort of breathed a sigh of relief and said, 'It looks like it's going south,'" Jones told SCIENCE NEWS.

The second California quake did not catch seismologists totally by surprise. Last year, Robert Wesson and Craig Nicholson of the USGS headquarters in Reston, Va., reported that this section of the Superstition Hills fault had remained noticeably quiescent in the last 20 years. "In a sense we predicted the position of the earthquake," says Nicholson. "But we had no indication of how soon or how late such an earthquake might occur."

The Alaska quake shook the ground for a full minute and sent thousands of people fleeing from low coastal areas. It did not trigger a major tsunami, or giant sea wave, as had been feared at first. *– R. Monastersky*

Hamster jet lag: Running it off

Scientists have noted that people who become "jet lagged" after long trips adjust more quickly to their new sleep-and-wake schedule if, upon arrival, they engage in outdoor activity such as walking or running. But it is unclear whether this resetting of daily biological and behavioral rhythms is a result of the activity itself, exposure to light, the traveler's conviction that exercise is beneficial or some combination of these factors.

Researchers at the University of Toronto now report that hamsters with simulated jet lag quickly adjust to their new timetable with the help of exercise alone. The finding, say Nicholas Mrosovsky and Peggy A. Salmon in the Nov. 26 NATURE, suggests that it may be possible to design exercise schedules that diminish jet lag among humans.

The investigators housed 20 male hamsters in a room with a cycle of 14 hours of light and 10 hours of darkness. During the dark period, a dim red light was kept on. After the hamsters became accustomed to the light-dark cycle and to running wheels in their cages, their day was suddenly shifted forward by 8 hours so that darkness arrived prematurely. Half were left undisturbed, while the others were removed from their cages 1 hour after the new onset of darkness and placed on unfamiliar running wheels. Three hours later they were returned to their home cages.

The simple experimental procedure resulted in a rapid adjustment to the new light-dark cycle. Hamsters, which are nocturnal creatures, began normal wheel-running following the onset of darkness after an average of only 1.6 days when they had the initial 3-hour running session. Undisturbed animals took an average of 5.4 days to adjust.

When the experiment was repeated without a dim red light during the dark period, undisturbed hamsters required an average of 11.6 days to adjust, compared with 1.5 days for those forced into activity.

The results suggest that, at least among people who are physically fit, appropriately scheduled jogging might be a good way to fight off jet lag, according to the researchers. Other research has indicated that drugs such as melatonin and the tranquilizer triazolam reduce jet lag.

The observed effects of exercise on "jet lagged" hamsters is surprising, writes ecologist Arthur T. Winfree of the University of Arizona in Tucson, in an accompanying editorial. But he says it is not yet possible to make specific exercise suggestions for similarly afflicted humans. He notes that the hamster data "dramatize our ignorance" of daily biological rhythms. *– B. Bower*