First Image from SPOT

On the evening of 21 February, the remote sensing satellite SPOT-1 was launched from Kourou, French Guiana, aboard the European Space Agency's Ariane rocket. Two days later it acquired the scene shown here as it passed over the Atlas Mountains in northern Algeria. The image clearly shows the tortuous geology of the area, and uses false color to highlight the various rock types. The northeast-trending ridges are hard sandstone, for example, while the yellow, fan-shaped areas are alluvial sands washed down from the mountains. Agricultural activities along the major wadis and streams show up as small red patches.

The launch of SPOT dramatizes the emergence of space remote sensing as a vigorous commercial enterprise. Images such as these will be marketed on a worldwide basis by SPOT Image, which is a venture of CNES, the French national space agency, together with 18 other public and private institutions in France, Belgium, and Sweden. The images themselves cover four spectral bands in the visible to near infrared wavelength region, and they offer a spatial resolution of 10 meters by 10 meters on the ground.

In the United States, meanwhile, the Earth Observation Satellite Company (EOSAT) of Landover, Maryland, has recently taken over commercial operation of Landsats 4 and 5, which were originally built and launched by the National Aeronautics and Space Administration. EOSAT is a joint venture of RCA and Hughes Aircraft. In addition to operating the existing satellites, EOSAT is planning a polar orbiting platform known as OMNISTAR to be launched by the space shuttle in late 1988 or early 1989—assuming, of course, that the shuttle will be flying again by then. Not only will OMNISTAR hold a wider variety of sensors than a conventional spacecraft, but with a design lifetime of 20 years it will last three to four times as long. Visiting shuttle astronauts will repair and upgrade the instruments as needed. EOSAT's agreement with the government calls for a $250-million federal subsidy during its first few years as it attempts to make the remote sensing business self-supporting. The White House zeroed out that appropriation in this year's budget request. However, Landsat commercialization has considerable support on Capitol Hill, and the company expresses confidence that Congress will put the money back in. ■ M. MITCHELL WALDROP

Briefing:

AIDS Drug Shows Promise in Preliminary Clinical Trial

A drug that disrupts the life cycle of the AIDS virus has shown promise in an early clinical trial.* Nineteen patients, who either had AIDS (acquired immune deficiency syndrome) or had symptoms suggesting that they were developing the disease, were given AZT (3′-azido-3-deoxythymidine) for 6 weeks. The primary goal of the trial was to determine whether AZT could be given to patients without causing unacceptable toxicity—and that appears to be the case. In addition, the results suggest that the patients' conditions improved somewhat while they took AZT. Nevertheless, study coordinator Samuel Broder of the National Cancer Institute cautions, "A 6-week study is not adequate to draw any conclusions about clinical efficacy."

The AIDS virus, which is called both human T-cell lymphotropic virus III (HTLV-III) and lymphadenopathy-associated virus (LAV), causes a severe immune depression by infecting, and eventually killing, the helper T cells needed for mounting many immune responses. The virus has an RNA genome that is copied into DNA in infected cells by a viral enzyme. AZT blocks this because cells convert the drug to a substance that resembles a normal DNA building block. The viral enzyme can add this substance to the growing DNA chain, but AZT's structure then prevents the addition of further building blocks, thereby interrupting the life cycle of the AIDS virus.

Although AZT, with its ability to terminate DNA synthesis, might have been expected to produce intolerable side effects, they proved to be relatively mild, as least during the short course of this trial. They included headaches and decreases in the white and red blood cell counts of the patients. No patients died of drug-related causes, but one dropped out because of a possible adverse reaction to AZT.

AZT's side effects may have been less severe than had been feared because the enzyme that synthesizes cellular DNA is more resistant to the drug than is the enzyme that synthesizes the viral DNA. "It is not as easily fooled into putting AZT into DNA," Broder explains. He notes that Jerome Horwitz of the Michigan Cancer Foundation in Detroit synthesized AZT in

*R. Yarchoan *et al*, *Lancet* **1986-I**, 575 (1986).
†H. Mitsuya and S. Broder, *Proc. Natl. Acad. Sci. U.S.A.* **83**, 1911 (1986).

the 1960's as a possible cancer drug, but that idea was abandoned when it failed to kill tumor cells.

The results of the current trial also show that AZT is effective when given by mouth, which is important for any drug that might have to be taken for a long time. Moreover, the drug can pass from the bloodstream into the central nervous system. The AIDS virus often infects cells in the brain, and a drug for treating AIDS would have to be capable of countering its effects there, as well as in the blood lymphocytes.

During the 6-week experiment, the patients had an average weight gain of about 5 pounds, which is one indication that the drug might produce clinical benefits. In addition, there were signs that AZT improves immune functioning. The numbers of helper T cells increased in 15 of the 19 individuals, especially when they were on the highest doses tested, and about one-third developed responses indicating some restoration of their cell-mediated immunity. Two individuals had spontaneous remissions of fungal infections under the fingernails while they were taking AZT, although three others developed mild, albeit treatable, infections. Finally, the virus could not be detected in lymphocytes from individuals who received the highest doses, a finding which suggests that AZT may suppress the virus as predicted.

Broder stresses the extremely preliminary nature of these results. Additional trials will be necessary both to determine whether AZT is as well tolerated in the long term as it was in the short term and to assess its clinical potential. David Berry of Wellcome Research Laboratories in Research Triangle Park, North Carolina, is currently organizing a rigorously controlled study that will include five to ten medical centers in the U.S. cities where AIDS cases are concentrated. Clinicians at the University of Miami Medical Center have already begun testing AZT.

Meanwhile, Broder and his NCI colleague Hiroaki Mitsuya have examined a series of compounds that are related to AZT to determine how their structures influence their abilities to inhibit HTLV-III infectivity.† "Very simple modifications give profound differences in the antiviral activities," Broder says.

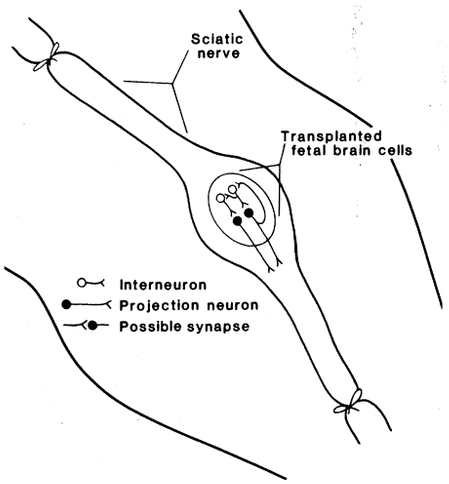
In general, the NCI workers find that the compounds must be capable of being converted into forms that can be incorporated into DNA but that prevent further growth of the molecule. Information such as this may aid in the design of new drugs for combating infection by the AIDS virus and perhaps by related viruses. ■

JEAN L. MARX

Fetal Mini-Brain in Peripheral Nerve

"It looks very much like a snake that has swallowed a pig," says Albert Aguayo of McGill University, describing a "mini-brain" preparation of fetal brain cells injected into an adult rat's leg nerve. Aguayo and Laurie Doering have just shown that fetal neurons will grow and differentiate for a while and then undergo specific degenerative changes, if they are transplanted and isolated in a leg nerve for long periods of time. Seeing the transplanted fetal brain cells degenerate after they appeared healthy for 3 months surprised Aguayo, who reported the findings at a recent meeting on neuroaxonal dystrophy and axonal transport.*

Doering and Aguayo devised the preparation to see if the fetal neurons would become like their adult counterparts when grown outside the brain. "We were looking for survival (of the fetal nerve cells) and were really surprised by the nature of the changes we saw," said Aguayo. "Some of the changes in these mini-brains were similar to those that occur in the aging human brain."



Aguayo and Doering *transplant fetal brain cells into the sciatic nerve of an adult rat's leg. The leg nerve bulges as transplanted cells grow and differentiate into a "mini-brain" that seems to contain short-fiber interneurons and long projection neurons. After 6 months, some mini-brain neurons die or show degenerative changes similar to those seen in aged or diseased human brains. [Adapted from a presentation by Albert Aguayo at the recent Neuroaxonal Dystrophy and Axonal Transport meeting.]*

The researchers took neopallium, a part of the fetal brain that will develop into cerebral cortex, out of rat embryos about 1 week prior to birth. They dissociated the cells and grew them in tissue culture for a few days before injecting the preparation into an adult rat's sciatic nerve.

"These transplants of cortex into the leg of an animal lack their normal brain connections and have no inputs from the spinal cord or brainstem. Also, the long projection neurons that would normally leave the cortex have nowhere to go," according to Aguayo.

Nevertheless, Doering and Aguayo find that transplanted fetal neurons differentiate to a state that is somewhat similar to adult brain cortical neurons. After 3 months, the researchers mark mini-brain neurons with antibodies that indicate specific substances, such as enzymes, peptide transmitters, or elements of cytoskeleton. Anatomical techniques as well as these antibody labeling techniques can distinguish interneuron and projection neuron populations in the adult cortex.

"As we looked at the transplants for longer periods of time, we began to see a series of changes," says Aguayo. After 6 to 12 months, some neurons show signs of degeneration similar to those in the aging or diseased human brain. For instance, an antibody called RT97 normally marks a special population of neurofilaments in nerve fibers, but does not stain cell bodies. "This reverses in the older transplants and the antibody begins to stain the cell bodies," Aguayo reports. A similar reversal of antibody staining occurs in brain tissue from dementia patients who had Alzheimer's or Pick's disease.

In the older transplants, Doering and Aguayo also saw abnormal structures, including spherical Hirano bodies, known to accumulate in diseased nerve fibers. Therefore, according to Aguayo, he and Doering " . . . have been able to demonstrate various degenerative changes in certain transplanted cortical neurons, as well as a gradual disappearance of these cells, in long-term preparations."

"What exactly the mechanisms for these changes are, and why the changes seem predominant in certain cells, is unknown. But it is now possible to create an experimental situation and ask if these changes can be exaggerated or prevented." Thus, the mini-brain may be a model for studying some degenerative neuronal changes associated with aging and disease as well as a model for the interactions of transplanted neuronal tissue with their targets. ■

DEBORAH M. BARNES

*"Neuroaxonal Dystrophy and Axonal Transport," 19–21 February 1986, National Institutes of Health, Bethesda, Maryland. The symposium was organized by the Fogarty International Center and the National Institute of Neurological and Communicative Disorders and Stroke.