Gene-Transfer Trial Begins in Humans

In the first step of a landmark experiment, government researchers gave genetically altered tumor-fighting cells to a cancer patient this week. The genetic manipulation isn't therapeutic, but is designed to help study a promising new cancer treatment. The action marks the first time scientists have given humans genetically engineered cells in an approved experiment.

Many scientists believe the trial heralds the beginning of a new era in biomedical research in which scientists will begin curing genetic disorders by inserting therapeutic genes in patients. Ultimately such work may lead to treatments for sickle cell anemia, cystic fibrosis and other inherited disorders.

Steven A. Rosenberg and R. Michael Blaese of the National Cancer Institute and W. French Anderson of the National Heart, Lung, and Blood Institute lead the historic experiment on ten patients with advanced melanoma, a deadly form of skin cancer. The researchers gave the first patient an injection of genetically altered tumor-infiltrating lymphocytes (TIL) – white blood cells that seek and destroy cancer cells – on May 22. They hope to complete giving similar injections to the remaining patients within 30 days, Rosenberg says. "We'll be studying these patients intensely," he adds.

The terminal cancer patients won't benefit directly from the genetic manipulation, but may benefit from the TIL therapy, which can shrink tumors. The impetus for the current experiment grew out of Rosenberg's previous experience with TIL therapy as reported last year in the Dec. 22 NEW ENGLAND JOURNAL OF MEDICINE. In that report, Rosenberg and colleagues treated 20 melanoma patients with TIL therapy, finding tumor regression in 11 of the patients.

TIL therapy aims at bolstering a patient's own immune response to cancer. The researchers harvest TIL cells, a key part of the immune system, from the patient's tumor, bathe the cells in a growth factor known as interleukin-2, and inject billions of TIL cells back into the patient's bloodstream where they home in on the tumor.

But preliminary work with TIL therapy raised questions about why the method works for some patients and not for others. To learn more about TIL therapy, the researchers designed the current trial in which TIL cells are marked with a gene that produces resistance to a neomycin-like antibiotic, a substance that kills human cells.

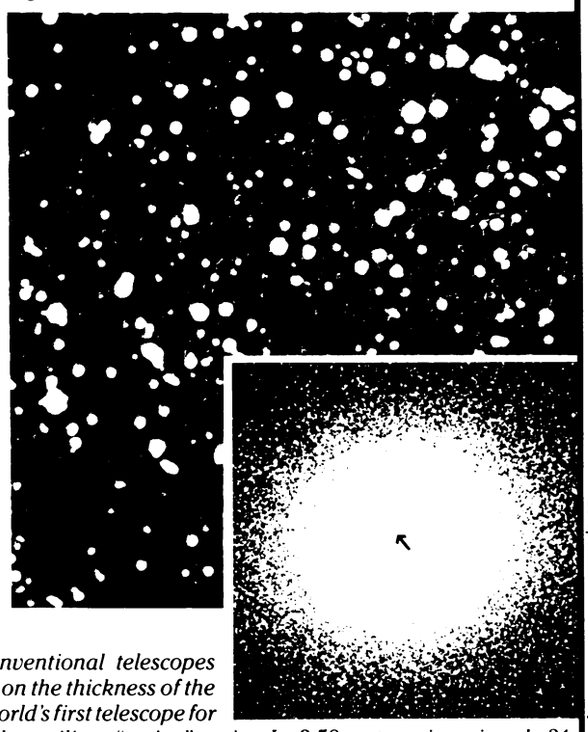
A weakened, nonvirulent mouse leukemia virus serves as a carrier to insert the gene into the chromosomes of TIL cells. The genetic marker allows scientists to track TIL cells as they wend their way through the body. The researchers identify the genetically altered TIL cells by taking blood and tumor tissue samples and exposing them to the antibiotic. The gene-altered TIL cells are the only ones that can survive.

The scientists already have taken blood samples from the first patient, but have not analyzed the results, Blaese says. The ultimate goal in the trial is to figure out what makes certain TIL cells potent cancer killers, he adds. Eventually, the scientists hope to identify specific genes responsible for tumor-fighting ability. Such work could lead to gene therapy that would bolster the body's ability to kill cancer, he says.

The precedent-setting experiment had to pass a rigorous review conducted by NIH's Recombinant DNA Advisory Committee, a panel of scientists, ethicists and lawyers that advise NIH on genetic engineering. The panel expressed concerns about whether the mouse retrovirus used to infect the TIL cells might cause disease in humans. The group gave its approval after reviewing evidence showing that the retrovirus had been crippled, rendering it harmless to people.

But NIH scientists faced another hurdle when the Foundation on Economic Trends, a Washington, D.C., advocacy group, filed a lawsuit asking the U.S. District Court for the District of Columbia to block the experiment (SN: 2/4/89, p.68). That lawsuit was settled May 16, paving the way for the first patient to receive the genetically altered TIL cells this week. The settlement orders NIH to hold all future deliberations on genetic engineering in public session, a move the agency contends is current policy. Jeremy Rifkin, president of the foundation, filed the suit claiming NIH scientists had made decisions on the gene-transfer trial in secret. – *K.A. Fackelmann*

A sharp, new eye scans the southern sky



European Southern Observatory

Stars in a globular cluster are packed so tightly that ordinary optical telescopes have trouble resolving individual stars. The European Southern Observatory's recently completed New Technology Telescope (NTT) in Cerro La Silla, Chile, has now produced probably the sharpest images of stars in a globular cluster ever obtained using a ground-based telescope. The false-color photograph is a computer-enhanced image of stars near the center of the bright globular cluster Omega Centauri (inset). This cluster, a satellite of the Milky Way galaxy, contains several million stars.

Whereas mirrors in conventional telescopes keep their shape by relying on the thickness of the glass used, the NTT is the world's first telescope for general astronomical use that utilizes "active" optics. Its 3.58-meter mirror is only 24 centimeters thick. Computer-controlled supports pressing against its back maintain the mirror's shape (SN: 3/19/88, p.188). The 10-meter Keck telescope now being constructed on Mauna Kea in Hawaii uses a similar principle.

The NTT saw "first light" on the night of March 23, when the image shown was captured in a 10-second exposure. Because the telescope concentrates light on the detector so effectively, astronomers can see fainter stars than with other telescopes. Depending on the sky background and the accuracy of tracking astronomical objects, even higher resolutions may be possible.