SCIENCE NEWS of the week

Gene Therapy Meets Liver Transplants

A ground-breaking proposal to seed the failing livers of desperately ill children with healthy, genetically marked liver cells cleared its biggest hurdle last week, receiving provisional approval from a key advisory subcommittee of the National Institutes of Health (NIH).

The experiment would assess the effectiveness of a new cell-transplant technique that could obviate the need for whole liver transplants in some patients. It could also be the first attempt to transplant patients with genetically altered cells that may persist in the body for life. Previous human gene therapy and marker gene experiments (SN: 12/22&29/90, p.388) have involved circulating blood cells, which die off after a few months.

The NIH's Human Gene Therapy Subcommittee conditionally approved the proposal — submitted by researchers at the Baylor College of Medicine and Texas Children's Hospital in Houston — to inject up to six patients with liver cells grown in the laboratory and marked with a gene for antibiotic resistance. The gene will allow the researchers to detect the transplanted cells. The researchers expect most of the patients to be children, because few child-sized donor livers are available for transplant.

"We really hope we can get some children through their liver failure and determine if the [cell] transplants work," says Fred D. Ledley, leader of the Houston team. The researchers have tested the cell transplant technique in animals, but the proposed trial will mark the first use of laboratory-cultured liver cells in humans.

Transplanting liver cells, or hepatocytes, could serve as an alternative someday to whole liver transplants in children too small to get livers from larger donors, Ledley says. It could also offer hope to the hundreds of U.S. children and adults each year who die of liver failure before a donor organ can be found.

The researchers plan to inject billions of the altered cells into the primary vein carrying blood to the liver. The marker gene will allow them to determine whether the hepatocytes take up residence in the liver and how long they last. The marker will not have a direct therapeutic effect, although it could help the researchers gauge how long to keep the patients on immune-suppressing drugs.

Eventually, Ledley hopes to adapt the treatment for children with liver-associated metabolic diseases by genetically altering hepatocytes to produce the protein their defective cells cannot.

Two of the nine NIH panel members voted against the Houston team's proposal, saying it had not proved to them the necessity of administering altered genes in order to determine whether the transplant method works. Panelist R. Scott McIvor, a geneticist from the University of Minnesota in Minneapolis, suggested that the researchers instead try to monitor the transplanted cells by looking for distinctive proteins on their surfaces. He also contended that the subcommittee needs more data demonstrating the team's ability to genetically tag human hepatocytes. In the end, the rest of the panel agreed to approve the proposal on the condition that the investigators provide the extra data before starting the experiment.

The Houston team must also win approval from the NIH's Recombinant DNA Advisory Committee, which meets May 31, and from the Food and Drug Administration. In addition, the researchers need the signed approval of the NIH director. "We think we'll be approved to start treating patients by the fall," Ledley says.

Three other gene-marker experiments won provisional approval at last week's subcommittee meeting. These include proposals by two separate teams — one at the St. Jude Children's Research Hospital in Memphis, Tenn., the other at Houston's M.D. Anderson Cancer Center — to use genetically tagged bone marrow cells to determine why some marrow transplants fail. The subcommittee also approved a proposal by researchers at the University of Pittsburgh School of Medicine to track tagged cancer-fighting cells infused into the bloodstream. — *C. Ezzell*

Lava cracks the seafloor-spreading code

For nearly 30 years, geologists have studied seafloor spreading, the volcanic process that creates the deep ocean floor. But for all their effort, they still know little about this important phenomenon, which churns out more than half of the Earth's surface crust.

That may change in the next few years. Researchers have now identified an actual eruption believed to be part of a seafloor spreading episode. Their finding opens up new possibilities for studying these planet-shaping events.

"This is the first documented case of a deep-water eruption on the midocean ridge system," says Robert W. Embley, a marine geologist with the National Oceanic and Atmospheric Administration (NOAA) in Newport, Ore. Embley discovered the eruption along with NOAA's Christopher G. Fox and William W. Chadwick Jr. of Oregon State University in Newport.

The three scientists made their finding while comparing two maps of the same area produced at different times. Information collected by deep-water cameras in 1989 revealed a low hill of young lava along the Cleft segment of the Juan de Fuca ridge, which runs offshore of Oregon and Washington state. But bathymetric sonar data from 1981 showed no hill at that time. This suggests an eruption occurred in the region sometime between the two surveys, the researchers assert in the April 4 NATURE.

Geologists have identified many other young volcanic deposits on the midocean ridges, but have been unable to tell whether the lava erupted last week or last century. The mapping data for the Cleft segment enabled Embley's group to bracket the region's eruption date between 1981 and 1989. Using other seafloor surveys, the Oregon scientists believe they can further constrain the dates to between 1983 and 1987.

The first mound they discovered measures 35 meters high and a kilometer in width. New eruptive features extend in a line from that mound for 16 kilometers.

The young rocks are pillow lavas, created when molten rock comes in contact with cold water. The lava has a shiny appearance and lacks a sediment cover. In some places, tubeworms have already established residency.

The researchers suggest that the recent eruption indicates an episode of subsurface seafloor spreading. According to theory, the spreading process occurs when two oceanic plates separate by several meters and molten rock rises to heal the crack.

The Oregon scientists think their findings also support speculations that seafloor spreading creates huge plumes of mineral-rich, slightly heated water. Oceanographers discovered these "megaplumes" in 1986 and 1987 while cruising in the Cleft region (SN: 10/10/87, p.238).

To catch any future action, Embley and his colleagues plan to install several types of instruments on the Cleft segment. Among other things, scientists want to know how often the ridge spreads and how large an area opens at once. "It seems like we're finally getting to the point where we'll get some answers to these questions," says Chadwick. — *R. Monastersky*