Biomedicine

Gene therapy approved for lung cancer

A National Institutes of Health panel last week approved the first use of gene therapy against the leading cancerous killer in the United States: non-small-cell lung cancer.

The panel voted to permit a team led by Jack A. Roth of the University of Texas' M.D. Anderson Cancer Center in Houston to inactivate a cancer-causing gene called K-ras in the tumors of lung cancer patients and to insert into the tumors a normal copy of a cancer-suppressing gene called p53. When mutated, p53 contributes to the chain of events that causes many types of cancer.

Roth and his colleagues received approval from the NIH Recombinant DNA Advisory Committee to use the new gene-therapy procedure to treat 14 patients with advanced lung cancer. After surgically removing as many of the patients' lung tumors as possible, the researchers plan to inject the remaining tumors with genetically engineered viruses containing two foreign genes. The first gene will direct the cancer cells to produce so-called antisense genetic material designed to shut down the action of K-ras (SN: 2/16/91, p.108). The second gene will replace a defective p53 gene in the tumors.

The researchers hope the procedure will arrest the growth of the patients' tumors and perhaps prolong their lives. Because non-small-cell lung cancer does not respond readily to surgery, radiation, or chemotherapy, many patients with the disease die within a year. In contrast, chemotherapy cures roughly 80 percent of patients with the less common small-cell lung cancer.

Barbara E. Murray of the University of Texas Medical School in Houston, who chaired the NIH panel, says the gene-therapy procedure "is a novel approach that offers a long shot for a group of patients with few other options."

Before beginning the treatment, Roth and his colleagues must also receive approval from the Food and Drug Administration. They met with FDA officials to apply for this approval last week.

Sneaking drugs past the brain's barrier

By incorporating a protein into a fatty molecule, pharmacologists can disguise the protein well enough to slip it through the specialized brain-protecting structure called the blood-brain barrier, which normally excludes proteins.

This strategy may offer a new means of sneaking drugs for chronic pain and other central nervous system disorders past the brain's sentry.

Nicholas Bodor and his colleagues at the University of Florida in Gainesville sandwiched a naturally occurring pain-relief protein called enkephalin between a fatty acid and a molecule that becomes positively charged in the presence of enzymes found in the brain. The researchers report in the Sept. 18 SCIENCE that the fatty acid enabled the hybrid molecule to pass through the oily blood-brain barrier. Moreover, Bodor's team found that when the molecule became positively charged on the other side of the barrier, the change prevented it from diffusing back out into the bloodstream.

Using a sensitive technique called mass spectrometry, the Florida researchers determined that once the hybrid enkephalin molecule was trapped in the brain, other brain enzymes stripped off its disguise, freeing the drug to perform its pain-relieving role. They proved this by showing that injections of the intact hybrid enkephalin molecule prevented a group of rats from reacting as strongly to a mildly painful stimulus as a second group given an inactive control compound.

Bodor's group projects that the strategy will yield "a future generation of high-efficiency neuropharmaceuticals." Next, they plan to design hybrid molecules that will not only ferry protein drugs across the blood-brain barrier, but also regulate the release of the drugs once in the brain.

Earth Sciences

Antarctic ice: Slippin' and slidin'

For those worried that global warming might send Antarctica's glaciers sliding into the ocean—raising sea levels and provoking massive coastal flooding—there may be good news and bad. A new study suggests rising temperatures may not have any immediate impact on the West Antarctic ice sheet, the area most prone to collapse. That's good. However, that same study indicates that the ice sheet behaves erratically, sometimes collapsing suddenly without regard to global temperatures.

In an attempt to predict the ice sheet's behavior, Douglas R. MacAyeal of the University of Chicago developed a computer model using data about the ice sheet's underpinnings. He ran his model for 10 consecutive 100,000-year cycles to simulate the impact of changes in surface temperatures and sea levels over 1 million years. MacAyeal was "shocked" to find that the ice sheet collapsed into the ocean at three irregular intervals — 190,000 years ago, 330,000 years ago, and 750,000 years ago. These collapses did not necessarily correspond with periods of surface warming. "Think of how a yo-yo would behave if you had an uncoordinated person operating it," MacAyeal told SCIENCE NEWS. "You'd have a sort of jerky, erratic behavior instead of a nice smooth action. That's what I saw."

MacAyeal's model uses recently obtained data about the layer of "till" beneath the ice. Till, a muck of ground-up rock and water, acts as a lubricant for the ice sheet, influencing whether it slides into the ocean, he says. The till apparently reacts unpredictably to both surface temperature and heating from inside Earth, MacAyeal reports in the Sept. 3 NATURE.

Polar researcher Cornelis van der Veen at Ohio State University in Columbus expresses skepticism about the till's role in the ice sheet's behavior. "In [MacAyeal's] model, the velocity of the ice stream is determined by the properties of the till," he says. "Our interpretations indicate that is not the case."

Exploding into an ice age

Scientists have considered it a coincidence that the largest explosive volcanic eruption of the past 2 million years occurred near the beginning of the last ice age. But a new computer study suggests this mammoth eruption about 73,500 years ago may have accelerated Earth's cooling.

The eruption of Toba on the Indonesian island of Sumatra lofted more than 1 billion tons of volcanic ash and sulfur gases 27 to 37 kilometers into the atmosphere, say Michael R. Rampino of New York University and Stephen Self of the University of Hawaii in Honolulu. This debris could have created a cloud that reduced the sunlight striking Earth's surface. To estimate the impact of the cloud on global climate, the researchers extrapolated from the known effects of smaller, more recent eruptions such as the 1815 Tambora eruption. Rampino and Self calculate that Toba's cloud could have caused average global temperatures to drop by 3°C to 5°C for two to three years.

Supposedly, airborne volcanics dissipate too quickly to start an ice age. But Rampino argues that eruptions may speed global cooling if glaciation is under way. Toba's "volcanic winter" could have induced additional cooling and "the extra 'kick' that caused the climate system to switch from warm to cold states," the researchers propose in the Sept. 3 NATURE.

Rampino and Self also suggest that Toba may exemplify a more general "feedback" relationship between volcanic activity and ice ages: The ice age then under way may have set off Toba's eruption by lowering sea levels, relieving pressure on the volcano. The ensuing eruption, in turn, hastened the cooling. They plan more modeling studies of volcanic debris in the atmosphere during global cooling, Rampino says.

V. Ramaswamy of Princeton University, in a commentary accompanying the report, urges a search of paleoclimatic records for any link between huge eruptions and past ice ages.