SCIENCE NEWS of the week

Gene, Biochemical Fixes Sought for CF

When it comes to cystic fibrosis (CF), three seems to be the magic number. Just three years ago, scientists pinpointed the faulty protein that causes people with the disease to produce thick mucous and sustain the lung and other organ damage that leads to an early death. Now, researchers report progress in three very different approaches to compensate for or correct this protein defect. In one, they demonstrated the feasibility of gene therapy as a treatment option in three CF patients.

Because of a genetic defect, people with cystic fibrosis lack functional copies of a protein called the cystic fibrosis transmembrane conductance regulator (CFTR), which works like a channel to control the flow of chloride ions in and out of cells. Thus cells produce a "dehydrated" mucous, says Michael J. Welsh, a Howard Hughes Medical Institute researcher at the University of Iowa in Iowa City. His team now reports that cells lining the noses of people with this disease do take up and use a transferred gene that makes normal copies of CFTR.

A second anti-cystic fibrosis approach calls for using one of the body's own chemicals to get another protein channel to make up for the nonfunctional CFTR protein, while the third would make better use of the defective CFTR protein.

Several research teams are developing gene therapies to compensate for the defective CFTR (SN: 12/12/92, p.405). Some, like Welsh's group, put copies of the gene responsible for the normal CFTR protein into genetically modified adenoviruses, which typically cause colds. The virus transfers the gene when it infects a cell.

Applying even small amounts of modified virus to the nasal lining of three CF patients restored the voltage indicative of normal chloride-ion movement, Welsh reported last week in Dallas at the North American Cystic Fibrosis Conference and in the Oct. 22 CELL. At that meeting, Ronald G. Crystal of the National Heart, Lung, and Blood Institute in Bethesda, Md., said he saw similar changes in four of his patients who underwent gene therapy.

Before researchers can demonstrate that this approach may actually treat cystic fibrosis, they must first increase the amount of genetic material transferred, transfer functional genes to the lining of the lungs, and ensure they have a safe and effective way to transfer the genes, Welsh cautions. Some researchers worry that the effective dose of adenovirus will pose safety risks, but these early results suggest otherwise, Crystal adds.

Taking a different tack, Richard C. Boucher of the University of North Carolina at Chapel Hill and his group have shown that in mice bred to develop symptoms of cystic fibrosis, the severity of disease varies from organ to organ depending on the amount of another channel protein produced by cells in these organs. Pilot studies indicate that a substance called uridine 5′-triphosphate (UTP) can help people with cystic fibrosis clear the thick mucous from their airways, Boucher's group reported at the Dallas meeting. UTP increases fluid flow by making an alternative channel active enough to make up for what CFTR fails to do, report Sheldon S. Miller at the University of California, Berkeley, and his colleagues in the Oct. 15 SCIENCE.

In many people with cystic fibrosis, the faulty gene results in the loss of one of the amino-acid building blocks that make up CFTR. And this causes newly made copies of CFTR to stick permanently to a protein that helps fold it into the right shape, reports Yiping Yang, a molecular biologist now at the University of Pennsylvania Medical Center in Philadelphia.

While at the University of Michigan Medical School in Ann Arbor, Yang and his colleagues observed that normal and defective versions of CFTR both form in a cellular compartment called the endoplasmic reticulum. The versions attach to a "chaperone" protein called hsp70 for folding. But the defective protein never lets go and therefore never leaves its birthplace to start working as a channel, they report in the Oct. 15 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. This defective version would work right if it could only get to the cell membrane, says Yang. So treatments that split hsp70 from CFTR should restore CFTR's ability to function, he theorizes. —*E. Pennisi*

Crash course on a comet bound for Jupiter

Weaver, T.E. Smith/NASA, STSci

Hubble image of Comet Shoemaker-Levy 9 fragments. White denotes highest luminosity, red an intermediate brightness.

Lined up like pearls on a string, some 20 comet-like fragments will slam one by one into Jupiter next July. The impacts will allow at least two spacecraft — Galileo and Voyager 2 — to observe directly the most powerful series of collisions ever predicted for the solar system.

On that much, astronomers agree. But the amount of energy unleashed by the fragments, known collectively as Comet Shoemaker-Levy 9, remains a matter of intense debate. That's because researchers don't know the size, and hence the kinetic energy, of any of the pieces, which were discovered last March and are thought to originate from a parent body ripped apart by Jupiter's gravity in July 1992 (SN: 6/26/93, p.410).

Several studies reported this week may help astronomers estimate the size of the largest fragments. Researchers described their findings during a crash course on Comet Shoemaker-Levy 9 — a marathon four-hour session at the annual meeting of the American Astronomical Society's Division for Planetary Sciences in Boulder, Colo.

At the meeting, Harold A. Weaver of the Space Telescope Science Institute in Baltimore presented several snapshots of Comet Shoemaker-Levy 9 taken on July 1 with the Hubble Space Telescope. Although the images represent the highest resolution of the fragments to date, astronomers still can't clearly distinguish the hard core of each body from its comet-like shroud of dust and gas. Weaver estimates that the highly reflective shrouds, known as comas, account for some 70 percent of the luminosity of the fragments in the Hubble pictures. By subtracting this estimated contribution, Weaver and his colleagues calculate that the largest pieces have a core no greater than about 5 kilometers in diameter — about half the size of early estimates.

The kinetic energy of each fragment is proportional to its mass, which in turn is proportional to the cube of the fragment's diameter. Thus, the smaller size indicated by the Hubble images suggests that the fragments might dump into the Jovian atmosphere only about one-eighth the energy originally calculated. Nonetheless, Weaver notes, the total energy unleashed would still equal about 100 megatons of TNT.

If the Hubble study provides a maximum size for the largest fragments of Shoemaker-Levy 9, another study, reported in the Oct. 21 NATURE by James V. Scotti and H. Jay Melosh of the University of Arizona in Tucson, may provide a