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.

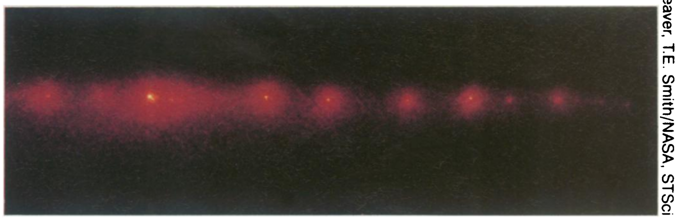
Before researchers can demonstrate that this approach may actually treat cystic fibrosis, they must first increase the amount of genetic material transferred, transfer functional genes to the lining of the lungs, and ensure they have a safe and effective way to transfer the genes, Welsh cautions. Some 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 minimum diameter. By tracing the orbits of the 20-odd fragments back in time, the astronomers infer that the parent body had a diameter of 2 kilometers. Thus the largest fragments might measure just 1 kilometer across and impart only one-thousandth the energy proposed in earlier studies.

At the meeting, Paul Chodas, Zdenek Sekanina, and Donald K. Yeomans of NASA's Jet Propulsion Laboratory in Pasadena, Calif., reported that their orbital calculations – based on a larger set of data – indicate that the parent body might have a diameter of 9 kilometers, consistent with the Hubble study. They predict that the Jovian collisions will take place over about five days, centered on July 21, 1994.

How often does a comet break into a string of pieces near Jupiter? According to Melosh and Paul Schenk of the Lunar and Planetary Institute in Houston, the answer may lie in Voyager 1 images of the large Jovian moon Callisto, which show 13 straight-line chains of craters. They say a string of cometary fragments sequentially striking the moon best explain these crater chains, as well as three others identified on the Jovian moon Ganymede. Schenk and Melosh estimate that comets with a diameter of a few kilometers break up near Jupiter once every 80 years. *– R. Cowen*

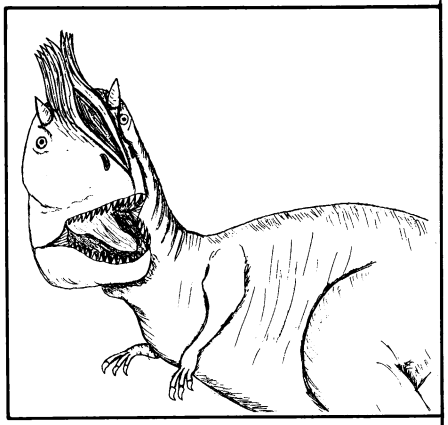
From Antarctica: The Elvis of dinosaurs

While it couldn't have crooned "Love Me Tender" or gyrated its hips, a new type of dinosaur discovered in Antarctica could have passed as a reptilian Elvis impersonator. This as-yet-unnamed beast from the Jurassic period sported an unusual head crest that swept upward in a style resembling the King's famous pompadour, according to the paleontologist who found the animal's skull as well as bones of another type of dinosaur during a 1991 expedition to the frozen continent.

"I called it 'the Elvis Presley of the Jurassic' because that's just what it looks like," says William R. Hammer of Augustana College in Rock Island, Ill. The dinosaurs found by Hammer and his colleagues are the first ones identified on the Antarctic mainland. Researchers have previously uncovered dinosaur specimens along the Antarctic Peninsula, which stretches toward the tip of South America.

Hammer described the discoveries last week at the annual meeting of the Society for Vertebrate Paleontology in Albuquerque, N.M. He collected the fossils from the flank of Mt. Kirkpatrick in the Transantarctic Mountains, about 650 kilometers from the present-day South Pole.

The Elvis look-alike belonged to a group of carnivorous bipedal dinosaurs known as theropods, which included the infamous *Tyrannosaurus rex*. The Antarctic animal's head crest was a thin layer of grooved bone that most likely served as a display, much like the tail of a male peacock, says Hammer. Although some theropods had crests running lengthwise along the snout, no other known theropod had a crest running perpendicularly across the skull.



William J. Hickerson

A rough illustration of the crested theropod discovered in Antarctica. Approximately 8 meters in length, the animal would have walked upright.

"It's one of the most bizarre theropods I've ever seen. That thing is really important," says Philip J. Currie of the Tyrrell Museum of Paleontology in Drumheller, Alberta.

Besides the crested theropod, Hammer and his colleagues also discovered the foot of a prosauropod dinosaur and the arm of a flying reptile called a pterosaur. The fossils date from the early Jurassic, sometime between 200 million and 175 million years ago. At that time, Antarctica had a far balmier climate and was farther away from the pole, although perhaps still within the Antarctic circle, says Hammer. *– R. Monastersky*

Avalanche dynamics: Dripping water drops

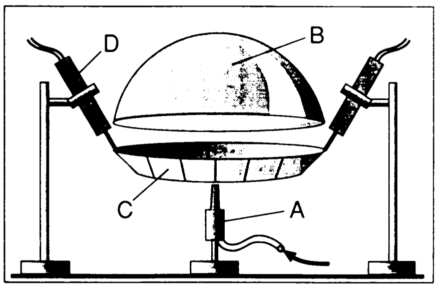
A hot shower in a cold bathroom can generate a thick mist of water droplets. Those droplets that collect on the bathroom window or mirror initially form a thin film on the surface. But over time, these droplets grow larger, coalesce, and begin to drip downward, engulfing other drops along the way.

Now, researchers have taken a closer look at this commonplace but rarely studied phenomenon of water-droplet "avalanches." The experiment was "the first of its kind," says physicist Franco M. Nori of the University of Michigan in Ann Arbor.

Nori and Michigan colleagues Britton Plourde and Michael Bretz describe their results in a paper scheduled for publication in the Oct. 25 PHYSICAL REVIEW LETTERS.

In recent years, researchers have studied avalanches and other collective effects in a variety of systems ranging from sandpiles (SN: 7/15/89, p.40) to regions of a material magnetized in different directions (SN: 3/31/90, p.207). But in these systems, the avalanches involved well-defined individual units, such as sand grains or magnetic domains.

Nori and his co-workers were interested in the dynamics of avalanches in which the units could grow in size. For water droplets continuously sprayed on a slanted surface, an avalanche occurs when individual droplets reach a critical mass, at which point they begin to run down the surface, capturing other droplets stationed along their paths.



Nori et al./Phys. Rev. Lett.

A forced-air mister (A) sprays distilled water upward into a transparent plastic dome (B). Spray droplets collect on the dome's inner surface, producing streams that run down and eventually drip off the rim. The falling droplets then hit and immediately run off a flexible, sloped ring (C) suspended beneath the dome. Pressure-sensitive detectors (D) measure how much each droplet impact stretches the ring.

It took the researchers nearly two years to design and construct an apparatus (see diagram) for measuring the size and duration of water droplet avalanches and the time between successive avalanches. In the end, they clearly demonstrated that their system shows the same kind of loading-unloading cycles that typify sandpile avalanches. Although water droplets are continuously deposited on a slanted surface, water runs off the surface at irregular intervals rather than continuously.

This effect proved particularly strong when the researchers used low spray rates and water chilled to near freezing. The lower temperature makes the water more viscous, which provides more cohesion between droplets, Nori says. This allows the droplets to gather into larger clusters, setting the stage for occasional huge avalanches that practically clear the surface. *– I. Peterson*