Cystic fibrosis flaw reversed *in vitro*

In separate laboratory efforts using cultured human cells, two research teams have corrected a cellular defect that causes up to 75 percent of cystic fibrosis cases. They accomplished this feat by inserting a gene that produces a normal protein, known as cystic fibrosis transmembrane conductance regulator (CFTR), into cells bearing a mutant gene that encodes an abnormal version of the protein.

Cystic fibrosis, an inherited disease, strikes one out of every 2,000 white children in North America and kills most of them before age 30. The new studies mark the first time scientists have engineered cells to produce normal CFTR. Last year, researchers isolated the defective protein and identified the mutant gene encoding it (SN: 9/2/89, p.149).

"The research is a milestone," says Robert Beall of the Cystic Fibrosis Foundation in Bethesda, Md. "It means that gene therapy [for this illness] is not a matter of if, but when."

In addition to gene therapy applications, the work suggests other novel ways to help treat cystic fibrosis, says Michael J. Welsh of the Howard Hughes Medical Institute at the University of Iowa in Iowa City, who coauthored one of the new studies. The ability to produce both defective and normal versions of the protein, he says, may enable researchers to identify CFTR's exact function. Scientists know that CFTR helps regulate the transport of chloride ions into and out of cells, and they believe that a flawed version resulting from genetic mutation slows that flow, leading to the thick mucus secretions that clog the airways and leave cystic fibrosis patients vulnerable to lung infections.

Once researchers elucidate the protein's structure, they might succeed in designing drugs to alter the flawed protein so that it no longer causes disease, Welsh suggests. He adds that an antibody test for the abnormal protein could speed disease diagnosis.

Welsh and co-workers from Tufts University School of Medicine in Boston and Genzyme Corp. in Framingham, Mass., used *Vaccinia* (cowpox) viruses to insert multiple copies of normal CFTR genes into cells cultured from the airways of a cystic fibrosis patient. Before gene insertion, the diseased cells could not activate a messenger chemical, known as cyclic AMP, to open chloride ion channels. After the researchers added copies of the normal gene, biochemical and electrophysiological tests demonstrated that cyclic AMP opened the channels and allowed ion transport, eliminating the cellular defect. Insertion of the mutant version of the gene did not open the chloride channels, the team reports in the Sept. 27 NATURE.

James M. Wilson of the Howard Hughes Medical Institute at the University of Michigan in Ann Arbor, with colleagues from the University in Alabama at Birmingham and the Hospital for Sick Children in Toronto, Ontario, achieved similar results using the same gene but a different virus and cell type.

Wilson says his group chose a retrovirus over the highly efficient *Vaccinia* because the retrovirus does not kill the cells it infects and thus allows investigators to study cell cultures indefinitely. (Cultured cells infected with *Vaccinia* survived about 24 hours — just long enough to show repair, Welsh notes.)

Wilson's group inserted single copies of the gene for CFTR into cultured pancreatic cells with the cystic fibrosis defect. In the Sept. 21 CELL, they report test results showing that the genetic addition repaired the abnormality. — *R. Cowen*

Magellan mapping Venus

The Magellan spacecraft started mapping the surface of Venus with radar on Sept. 15, about two weeks later than planned. But the mission, due to last 243 days — or the time it takes Venus to make one rotation about its axis — got off to a shaky start when Magellan's communications with Earth twice mysteriously shut down.

Since reaching Venus on Aug. 10, Magellan has settled into a stable orbit, now circling the planet every 3.26 hours. It gathers mapping data about eight hours a day. When it's not bouncing radar signals off Venus' surface, the craft turns toward Earth to play back its cartographic measurements and provide engineering data about the state of its health.

During a shakedown phase — prior to the craft's beginning full-time mapping — project officials played back to Earth some preliminary radar images and engineering data stored on Magellan's two tape recorders. Researchers are now combing through this complete "data dump" looking for clues to why the craft subsequently twice fell mute. The craft inexplicably lost contact with Earth for nearly 15 hours on Aug. 16 and again for 17 hours on Aug. 21.

With the radar-mapping images starting to emerge, Magellan officials say the mapping is "going well." They acknowledge, however, that they still do not know what caused the two communications problems, and that they cannot rule out another signal loss.

Ultimately, Magellan scientists hope to complete five radar scans of the entire planet — each time from a slightly different angle. Their goal is to collect enough data to eventually construct three-dimensional stereographic images of the Venusian surface. □

X-ray snapshots of 'solid flame' events

Put a match to the tip of a Fourth of July sparkler. A dazzling display of light immediately begins inching down the shaft as the searing heat sparks successively lower regions into combustive action. Researchers have now recorded with unprecedented detail the rapid material changes that occur during related "solid flame" reactions lasting mere seconds or minutes.

For more than 20 years, materials scientists — primarily in the Soviet Union — have explored the chemistry, physics and technological promise of such reactions, also known as self-propagating, high-temperature synthesis (SHS) reactions. Already, researchers have harnessed these "solid flames" to process solid ingredients directly into metallic alloys, composite materials and even superconducting ceramics.

Using one of the world's most intense synchrotron radiation sources, at Brookhaven National Laboratory in Upton, N.Y., a team led by Joe Wong of Lawrence Livermore (Calif.) National Laboratory has assembled crystallographic SHS snapshots. Scientists routinely compare starting ingredients against products formed after a reaction occurs. "But before synchrotron radiation, we never had the possibility of observing what happens during these [SHS] reactions," Wong says.

The researchers first compress combustible mixes — say, titanium, carbon and nickel powders — into blocks the size of ice cubes, which they place inside a crystallography chamber. Then they ignite the reaction as an intense beam of synchrotron X-rays bathes the sample. Detectors record the resulting diffraction patterns at intervals as brief as a tenth of a second. In a synchrotron, highly accelerated electrons copiously emit X-rays as they travel in bending paths.

In the Sept. 21 SCIENCE, the Livermore team displays several series of rapid X-ray diffraction scans taken both while and after the fast-moving reaction fronts of SHS reactions pass through samples. Viewed in sequence, these images indicate exactly when specific components undergo physical and chemical changes such as melting, crystallizing and forming alloys or ceramics.

SHS reactions can yield solid products requiring little postproduction machining and generate less waste material than conventional furnace processes, which take hours or days. Materials scientist James W. McCauley, dean of the New York State College of Ceramics at Alfred University, says he expects the more detailed pictures of these reactions to help researchers design better SHS recipes.

— *I. Amato*

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