Scientists are going to discover many subtle genetic factors in the makeup of human beings. . . . Once we can say that there are differences between people that are easily demonstrable at the genetic level, then society will have to come to grips with understanding diversity—and we are not prepared for that.
David Baltimore, American microbiologist, 1983

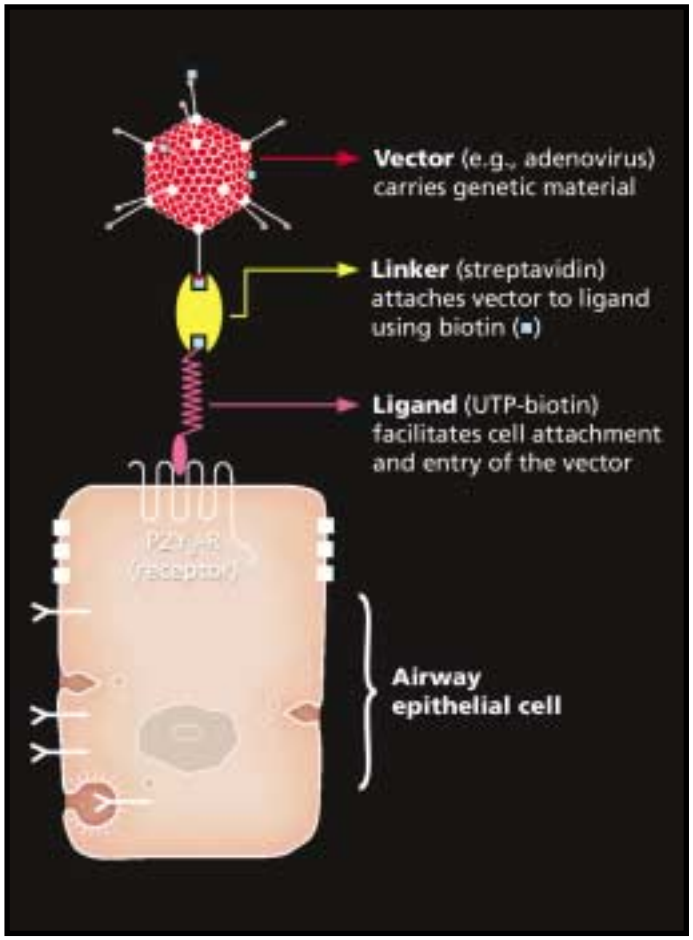
RESPIRATORY DISEASE

Gene Therapy for CF

New research on gene replacement therapy offers the hope of a cure for cystic fibrosis (CF). This fatal disease, symptomized by coughing, wheezing, lung infections, very salty sweat, and excessive appetite with inability to gain weight, affects about 30,000 Americans.

CF manifests when a person receives a mutated copy of the *CFTR* gene from both parents. More than 10 million people carry one copy of the defective gene. Most CF patients die in childhood, but some live into their 30s or 40s. Advances in drug therapies and other treatments such as lung transplants have improved the quality of life of CF patients in recent years, but still do not offer a cure.

Because lung infections are responsible for most CF fatalities, research into gene therapy for treating the disease has initially focused on replacing the mutant genes in the epithelial cells lining the lungs and nasal passages. But the human body has evolved a complex system to prevent invasion of foreign DNA, and the lungs have a particularly strong defense system. So scientists need to find a way to "trick" the cells into accepting replacement genes. In a report in the June 2000 issue of *Nature Biotechnology*, Silvia M. Kreda, a clinical research associate of medicine at the University of North Carolina at Chapel Hill, and colleagues describe research with a particular type of airway receptor molecule that may offer a reliable pathway into cells.



UTP-based conjugates for gene replacement therapy. Scientists have found that the $P2Y_2$ receptor is a viable target for gene therapy vectors seeking to transport a payload of healthy genes into airway passage tissues of CF patients.

Silvia Kreda, Reuther/EHP

Instead of producing the normal protein that forms channels in cell membranes for the passage of salt out of cells, people with CF produce a faulty protein, which causes a thick mucus that impairs function of the lungs, intestines, and other organs. If healthy genes can be transferred into the CF patient's cells, theoretically they should produce the protein product necessary to form the channels for proper electrolyte transport out of the airway cells.

Kreda and colleagues identified the $P2Y_2$ molecule receptor on the membrane surface of the lungs as a potential target for shuttling healthy genes into the airway passages. Their research strategy was to combine the nucleotide UTP, which binds to certain receptor molecules on the outside of the epithelial cells, with a commonly used vector known as an adenovirus. Using reporter genes to signal a successful transgenic event, Kreda's group demonstrated that UTP linked to the vector and facilitated its uptake into the cell. Additional experiments revealed that when UTP was linked to an adenovirus vector, *in vitro* transfer of the reporter gene into human lung cells was successful.

Kreda emphasizes that her lab is working on a model system for improving entry mechanisms in gene replacement. Before clinical trials with humans can be considered, however, vector construction needs to be refined for improved efficiency. Richard C. Boucher, the principal investigator for the study, says that although UTP is effective at binding to receptor sites on the membrane, it is rapidly degraded by the body's enzymes and is therefore not efficient for delivering the gene payload. Future *in vitro* experiments using the *CFTR* gene will measure channel activity to determine gene therapy's ability to correct the mutant gene. When the *in vitro* system is perfected, efficacy will be tested in animal models. A reporter gene will be transferred via the adenovirus vector into normal mice to verify gene expression. Then the *CFTR* gene will be introduced into knockout mice to determine whether the corrected gene is accepted into live cells in the respiratory tract.

The adenovirus, a DNA-containing virus that causes upper respiratory tract infections, is widely used as a vector in CF research because it is an established model that works well. It can pose a danger of infection to patients, however, and research is ongoing to address the safety issues of using adenovirus vectors in human studies, and to find safer vectors for gene replacement therapy. In September 2000, a panel of the American Association for the Advancement of Science called for a moratorium on gene-altering research and for the government to establish an oversight board as soon as possible. **–Mary Eubanks**

NEUROLOGY

Pulling the Plug on POPs

Officials from the United Nations announced on 10 December 2000 that representatives from 122 countries have agreed on the text of a treaty banning or sharply restricting the use of 12 highly toxic chemicals known as persistent organic pollutants (POPs). The treaty will be formally adopted during a diplomatic conference in Stockholm, Sweden, to be held 22–23 May 2001. After this, governments will ratify the treaty. The treaty will go into force once 50 nations have ratified it, a process estimated to take 3–5 years.

POPs travel easily through the environment and break down slowly. They have been linked with cancer, allergies, central and peripheral nervous system damage, immune disorders, birth defects, and other adverse effects, and can be transferred from mother to child through breast-feeding. In a 10 December 2000 press release by the United Nations Environment Programme, which organized the talks, session chairman John Buccini said, "Persistent organic pollutants threaten the health and well-being of humans and wildlife in every region of the world. This new treaty will protect present and future generations from the cancers, birth defects, and other tragedies caused by POPs."

The six-day session was held in Johannesburg, South Africa. It was the fifth time that diplomats met to work on guidelines for addressing POPs pollution at an international level. The treaty establishes control measures for the production, import, export, disposal, and use of an initial list of 12 highly toxic POPs, the so-called "dirty dozen." Eight of the chemicals may no longer be produced or used once the treaty goes into effect.

Exceptions have been granted for DDT, polychlorinated biphenyls (PCBs), dioxins, and furans. Until safer solutions can be developed, DDT may still be used in certain nations to combat malaria-carrying mosquitoes. PCBs will still be around in the form of electrical equipment such as transformers, which benefit from the chemicals' excellent dielectric properties. Governments will have until 2025 to arrange for PCB-free replacements. Finally, because dioxins and furans are unintentional by-products of burning and industrial processes, they are harder to control. Governments are therefore being asked to reduce their releases with an eye toward eventually eliminating them altogether.

The treaty is intended to be a flexible policy tool that can be expanded and updated in the future as needed. A POPs Review Committee will regularly consider other POPs candidates for control to ensure that the treaty reflects the state of the science.

–Susan M. Booker

POPs to Go

Aldrin (pesticide)

Chlordane (pesticide)

DDT (pesticide)

Dieldrin (pesticide)

Dioxins (burning/industrial by-products)

Endrin (pesticide)

Furans (burning/industrial by-products)

Heptachlor (pesticide)

Hexachlorobenzene (pesticide and industrial chemical)

Mirex (pesticide)

Polychlorinated biphenyls (industrial chemicals)

Toxaphene (pesticide)

Top to bottom: Corel Photo Disc

Virus Targets Amphibians

On 8 August 2000, USGS scientists announced their finding that an emerging iridovirus disease is partially to blame for a large die-off of western tiger salamanders in North Dakota. The same disease has also been linked to declines in the populations of multiple amphibian species in the Midwest and in eastern sections of the United States.

USGS researcher David Mushet says the recent die-off is the first amphibian mortality event due to disease recorded at the U.S. Fish and Wildlife Service's Cottonwood Lake Study Area of North Dakota since data gathering began in 1967. The scientists are working to establish whether the localized die-offs are part of a long-term worldwide amphibian decline that is only now being uncovered due to a greater emphasis being placed on amphibian population surveillance in recent years.

Protecting Parks from Pollution

Continued declining air quality in U.S. national parks prompted officials at the Department of the Interior to draft a letter to the EPA on 19 July 2000 requesting that the agency adopt a general regulation to protect resources within parks from the effects of air pollution. These effects range from decreased visibility to plant damage caused by nitrous oxide and other pollutants.

The National Parks Conservation Association, a watchdog organization, has found that visibility in the Great Smoky Mountains National Park has been reduced from its historic 93 miles to as low as 15 miles during recent summers. The group also says that much of the ozone pollution within the parks is coming from motor vehicles, and that the EPA is not regulating such pollution strongly enough.

Fool's Gold Mining

Millions of dollars' worth of gold has been illegally extracted from a gold mine in the Manado area of Indonesia, according to a 31 July 2000 BBC news report. Trespassing miners use large quantities of mercury to separate gold from surrounding materials. Toxic by-products of this process are dumped directly on the soil. An estimated 200 metric tons of mercury was released in the area during the first half of 2000. Environmental scientists have determined that mercury has made its way into nearby waters, which the local population of 400,000 depends on for food and fishing income.

HONORS AND AWARDS

Awards Remember Rall

Two new awards pay tribute to David P. Rall, the former NIEHS and National Toxicology Program director, who died in September 1999. Rall was a pioneer in the field of environmental health science, and is widely hailed for his work as an advocate for incorporating science-based prevention into public health policy.

In November, Eula Bingham, a professor of environmental health at the University of Cincinnati College of Medicine, received the David P. Rall Award for Advocacy in Public Health from the American Public Health Association. Bingham worked as assistant secretary of the Occupational Safety and Health Administration from 1977 to 1981. The award recognizes Bingham for her outstanding record of accomplishments in fighting to protect workers, consumers, and citizens from the danger of environmental and industrial disease. She was instrumental in the passage of the first community right-to-know program, in Cincinnati, which allowed workers access to their company medical records and records of toxicants in the workplace, and also called for chemical labels and worker education programs to help employees understand the labels.

"[Bingham's] scientific and ethical standards have always been of the highest order, and her dedication to and outspokenness on occupational health issues during her long career . . . have always been an inspiration to me and to many of her students and colleagues," says John Bucher, deputy director of the NIEHS Environmental Toxicology Program.

Stuart Bondurant, a professor of medicine and dean emeritus of the University of North Carolina at Chapel Hill School of Medicine, was honored in October with the David Rall Medal, given by the Institute of Medicine for particularly distinguished leadership as a chair of a study committee or similar activity. Bondurant is past president of the Association of American Medical Colleges and the former acting president of the Institute of Medicine.

In his years with the Institute of Medicine, Bondurant exhibited outstanding leadership as the chair of committees on controversial and highly visible topics, the selection committee said, citing his objective, balanced, and skilled work on groups studying the safety of silicone breast implants and the science base for tobacco harm reduction.

Bondurant says he has "unqualified respect" for Rall, and adds, "Many of the things we do today are legacies of his wisdom." **–Lindsey A. Greene**

INFECTIOUS DISEASE

Too Clean for Comfort

A research survey of liquid and solid soaps from across the country reveals that 45% contained antibacterial agents—chemicals that scientists say may not benefit human health but might instead create stronger bugs. In a presentation at the annual meeting of the Infectious Diseases Society of America in September 2000, Eli N. Perencevich, a research fellow in infectious diseases at Beth Israel Deaconess Medical Center in Boston, and colleagues described how they went through the lists of liquid and solid soaps sold in 23 national and local stores to see how many of them contained antibacterial agents.

Greenwell/EHP

Perencevich and colleagues examined 395 national brand liquid soaps and 733 bar soaps on display at stores in 10 states across the country. They found that 76% of the liquid soaps contained triclosan and about 30% of the bar soaps contained triclocarban. "Recent research into the action of triclosan has raised the concern that these products may encourage resistance to triclosan and other microbial agents," Perencevich says. "With so many of these products on the market, consumers may not realize they are purchasing soaps that contain antimicrobials. Perhaps people should check the products' ingredients closely when they make their next soap purchase."

"Although triclosan has been used as an antimicrobial for many years, it's only recently that we have learned how it acts on bacteria," says Stuart Levy, a professor of molecular biology at the Tufts University School of Medicine in Boston and president of the Boston-based Alliance for the Prudent Use of Antibiotics. "There is a specific gene in *Escherichia coli* and many other bacteria that produces an enzyme to make the cell wall. Triclosan disrupts the enzyme so that the bacteria can't make the cell wall, and therefore, cannot replicate." According to Levy, if there is a mutation in this gene, it may lead to bacteria that are resistant to triclosan or other antibiotic agents. "Triclosan doesn't cause a mutation," he says, "but by killing normal bacteria it creates an environment where the resistant, mutated bacteria are more likely to survive."

"No one has ever been able to prove that using antibacterial soaps meant that anyone was better off than those using standard soap," says Perencevich. "There has been no scientific data published to support the claim that adding these compounds to household products prevents infection. However, there are studies that suggest use of such products kills off the sensitive bacteria, leaving hardier bacteria such as *E. coli* and *Staphylococcus aureus*, which could be detrimental to health." Perencevich adds, "The fear is that use of these products will result in bacteria that live longer."

That fear may be misplaced, contend industry representatives. "The rising incidence of antibiotic drug–resistant bacteria is a serious worldwide concern," says Jerry McEwen, vice president for science at the Cosmetic, Toiletry, and Fragrance Association, based in Washington, D.C. "There is no real-life evidence that antibacterial products—as they are normally used in hospitals, in food preparation, and in people's homes—contribute to bacterial resistance." He continues, "While some studies have shown that antibacterial ingredients may promote resistant bacteria, these studies have been done under controlled laboratory conditions that do not reflect what happens to bacteria that consumers encounter in the real world."

Nevertheless, says Perencevich, "The magnitude of the availability of antibacterial soap products that we documented in our survey is cause for concern. This study suggests that further surveillance and study of triclosan resistance is warranted." **–Ed Susman**

Human Genome Project Information

The Human Genome Project (HGP) began in 1990 as a collaboration of the U.S. Department of Energy (DOE) and the National Institutes of Health (NIH). The project's goals include designing detailed genetic and physical maps of the human genome to determine the complete nucleotide sequence of the three billion base pairs that comprise human DNA and to identify the estimated 100,000 genes within the human genome. While developing tools for data analysis, the project also aspires to store this information in a database.

To provide both background and updates on this ambitious undertaking, the DOE and the NIH have established the HGP Information Web site, located at **http://www.ornl.gov/hgmis/**. The site hosts HGP resources ranging from answers to basic questions like "what is a genome" to information on the project's latest discoveries.

Under the Project Information heading, visitors can click on What's New to read the continuously updated Genetics in the News or the Research Digest, which announces consortia and recent research developments. The Media Guide link leads to basic and background information, including Genetics 101, a fact sheet explaining the DOE's involvement in the HGP, a link to the National Human Genome Research Institute home page, information on goals and grants, and a glossary of genetic terms. This link also leads to a genome image gallery.

More technical information is available through links under the Research heading, including resources on sequencing, mapping, instrumentation, and informatics with HGP updates. The Research in Progress link leads to Web sites that display the entire working draft sequence of the human genome and provide tools for its use. The U.S. & International Research Sites link leads to other research organizations that have contributed to genetic research. The Chromosome Launchpad link directs visitors to gene maps, sequences, and associated genetic disorders for individual chromosomes. And the BACs [Bacterial Artificial Chromosomes] link accesses a database that is the preferred clone resource for generating draft sequences of the human genome.

The Educational Resources section provides background publications, videos, posters, teaching aids, and bioscience career resources for students and teachers. For information on gene testing, genetic counseling, and the various tests available, users can click on the Medicine section. Here, health care providers can also explore links related to continuing medical education in genomics and other professional resources.

Various articles on genetic privacy, discrimination against gene therapy, and genetics in the courtroom are referenced under the Ethical, Legal, and Social Issues heading, which mentions that 3–5% of the HGP's annual budget goes toward studying the ethical, legal, and social implications surrounding the availability of genetic information. This represents the world's largest bioethics program, a model for programs around the world. **–Lindsey A. Greene**

Top to bottom: PhotoDisc, Reuther/EHP; Desk Gallery

The Amazing Dissolving Computer

Cornell University materials scientists have developed a new epoxy called Alpha-Terp that could lead to 100% recycling of computers. Currently, only about one-quarter of the circuit boards from the more than 20 million computers disposed of annually are broken down into recyclable parts because they are sealed with super-strong epoxy adhesives that prevent them from being totally disassembled.

When heated to 374°F, the new epoxy's chemical bonds begin to break down. It can then be dissolved with a common industrial solvent to allow repair or dismantling of the circuit board. The new epoxy was reported at the August 2000 meeting of the American Chemical Society.

Shocking Food Treatment

Electrolyzed water, produced by applying an electric current to a dilute saltwater solution, may serve a variety of food treatment purposes, according to University of Georgia scientist Yen-Con Hung. Devices to produce electrolyzed water are manufactured in Japan but have not yet made their way onto the U.S. market.

Electrolyzed water is highly acidic. Chlorine is produced when the electric current passes through the saltwater solution. According to Hung, the chlorine and other unidentified oxidant by-products kill bacteria more effectively in some cases than either heat or chlorinated water alone. In tests, the electrolyzed water killed bacteria without changing foods' color or smell. Hung found that soaking cutting boards in warm electrolyzed water for just five minutes reduced bacteria by up to one millionfold.

Hung plans to test electrolyzed water on chicken to see if it kills *Salmonella* and *Campylobacter* on poultry carcasses. He also plans to test the water on hard-to-treat products such as oysters.