

"Still
The Second
Best Thing
About Payday"

The NIH Record

Salute to NIGMS

'Basic Research Institute' Marks 30th Anniversary

This month, the National Institute of General Medical Sciences celebrates its 30th anniversary. NIGMS supports primarily basic biomedical research that is not targeted to the solution of particular diseases or to specific life stages.

This has been true since the institute's inception. The authorizing legislation, passed on Oct. 17, 1962, established the institute "for the conduct and support of research and research training in the general or basic medical sciences and related natural or behavioral sciences that have significance for two or more other institutes of NIH or are outside the general areas of responsibility of any other institute."

Research Training

It is important to note that research training, mentioned in the legislation that created the institute, is and always has been a vital part of the NIGMS mission. Well-trained new talent is essential to ensure the continuing generation and exploration of fresh ideas in biomedical research.

Over half of all NIH predoctoral trainees, as well as many postdoctoral trainees, receive their support from NIGMS.

In addition to its longstanding interdiscipli-

nary research training programs, NIGMS has several programs that address special areas of critical scientific need. These include biotechnology, molecular biophysics (with a focus on the interdisciplinary training needed for research on AIDS), the chemistry-biology interface (aimed at providing biological training for chemists and training in chemistry for biologists), a postdoctoral intramural program that provides training in pharmacology, and an integrated curriculum of scientific and medical study leading to the combined M.D.-Ph.D. degree.

NIGMS is also dedicated to increasing the number of scientists who are members of minority groups that are presently underrepresented in biomedical research. Toward this end, the institute sponsors special research and research training programs for students and faculty members at institutions with substantial minority enrollments through the Minority Access to Research Careers (MARC) and the Minority Biomedical Research Support (MBRS) Programs. These programs have helped thousands of minority students pursue undergraduate and graduate degrees and have enhanced research and

(See ANNIVERSARY, Page 8)

CFC Kickoff Emphasizes Everyone's Vulnerability

There are a number of familiar phrases to express the feeling—"There, but for the grace of God, go I...Oh, by what a fragile thread we hang..."—but the notion that our comfortable self-sufficiency, our lack of dependence on others is, indeed vulnerable, marked NIH's opening of the annual Combined Federal Campaign on Oct. 14.

Keynote speaker Dr. John Diggs, NIH deputy director of extramural research, called to mind the residents of South Florida before Hurricane Andrew hit; none of them expected their lives to be disrupted so thoroughly. None of them expected to rely on the charity of their neighbors.

"Tragedy can strike our lives in a matter of moments," he warned. "Give a little bit of extra thought this year when you make your contribution to CFC," he said. "Remember that trouble is just one Andrew away. Sometimes it comes in the form of a person, or an illness, or some other kind of crisis. And CFC will be there for you because you gave."

Many NIH'ers turned out on a warm, Indian summer noontime to hear marching bands from Wootton and Wheaton high schools, participate in the walk/run sponsored by Health's Angels Running Club and R&W, eat lunch outdoors, and browse among a series of tables set up by CFC-eligible organizations, of which there are some 300 more this year than

last. The tabletops were covered with a variety of promotional items available to passersby, including t-shirts, pencils, brochures, water bottles, and lapel buttons. One outfit advocating population control distributed flyers into which condoms were discreetly tucked.

Also speaking was Dr. Philip Schambra, director of the Fogarty International Center, which is host institute of this year's CFC campaign. Recalling Ben Franklin's warning that "we must all hang together, or we shall

(See CFC KICKOFF, Page 6)



Dr. John Diggs, NIH deputy director for extramural research, delivers the keynote address launching the 1992 Combined Federal Campaign at NIH.

Heroic Milieu of NIH

Killers Square Off In Mystery Book

By Rich McManus

Dr. Steven A. Rosenberg would like to go down in history as a serial killer—of cancer cells, cancer deaths and cancer misery. Best known as chief of NCI's Surgery Branch for the past 20 years, he has written a book that casts his NIH career in terms of a detective mystery, one prompted early in his training when the startling case of a man whose cancer-ridden body somehow cured itself gave Rosenberg the notion that the human immune system can recognize and kill cancer.

In the intervening years, Rosenberg has pursued relentlessly the idea of immunotherapy—marshalling the body's own immune system, through ever more sophisticated means including, now, gene therapy, to fight otherwise terminal cancer.

The book, *The Transformed Cell, Unlocking the Mysteries of Cancer*, is in many ways a paean to NIH, lauding, along its 336 pages, many NIH employees, the NIH itself, and perhaps most importantly, the desperately ill patients for whom the Surgery Branch offered the last, best hope for a cure.

(See ROSENBERG, Page 4)

NIH Grantees Win 1992 Nobel Prize in Medicine

Two NIDDK-supported scientists, Dr. Edwin Krebs and Dr. Edmond Fischer, have won the 1992 Nobel Prize in Physiology or Medicine.

The scientists, both with the University of Washington in Seattle, will share the \$1.2 million prize for their work on the regulation of cell activities by enzymes, a process that has major implications in the understanding and treatment of diseases ranging from diabetes to cancer.

The Nobel Prize culminates 40 years of collaboration between Krebs and Fischer, who view their discovery as an accidental one that was later found to be of tremendous importance in the regulation of all cell activities.

"We stumbled on it," Fischer said to the Associated Press. "We had no idea how widespread this reaction would be. Then over the years many, many people working in this area have developed the field and now we know that it's involved in just about every reaction inside the cell."

Beginning in the 1950's, the scientists began work that would lead to their discovery of a class of enzymes called protein kinases. The enzymes activate other proteins that perform various functions in the cell, including cell growth and death, hormone release, and muscle

(See NOBEL LAUREATES, Page 6)

Gene Disruption Linked to Leukemia

In their mission to construct a molecular map of human chromosome 11, Human Genome Project researchers have uncovered a genetic region that appears to be broken in some patients with leukemia—cancer of the white blood cells. Further analysis of the region suggests that the breakage disrupts the proper functioning of a gene that regulates the activity of other genes during development.

The work is reported in the October issue of the scientific journal *Nature Genetics*.

Researchers at the Salk Institute in La Jolla, Calif., discovered the gene while constructing a type of chromosome map, known as a physical map, of chromosome 11. The map covers a region of the chromosome that often breaks and exchanges pieces with other chromosomes in patients with leukemia. This swapping process, known as translocation, occurs in more than 75 percent of leukemia cases among infants younger than 12 months.

Translocations with chromosome 11 are common in patients with leukemia, cancer of the white blood cells. Team leader Dr. Glen Evans and his coworkers at Salk and at the Imperial Cancer Research Fund in England, studied chromosomes obtained from patients with acute lymphocytic leukemia or acute myelocytic leukemia. Acute leukemias account for almost all the leukemia cases among children and young adults. Leukemias arise in immature white blood cells, which become abnormal and grow and divide rapidly.

In the process of constructing the map, the researchers isolated a piece of DNA that spanned the region of chromosome 11 designated 11q23, a point where the chromosome is frequently found to be broken during leukemia-related translocations. They then sequenced the units of DNA that spanned the broken region to determine what genetic information might be carried there. Comparison of DNA in the

broken region with other DNA sequences stored in computer databases showed a sequence that was similar to a known gene found in the fruit fly.

"The discovery of this gene shows why model organisms are so important to the study of human genes," says Evans. "Since we know what the gene does in fruit flies, we can make a pretty good guess about what it does in humans. This will help us tremendously in focusing our work on understanding how this gene functions in leukemias and other developmental disorders."

Scientists had already discovered that the fruit fly gene, known as *trithorax* (*trx*), instructs cells to produce a protein that regulates the function of DNA. The *trx* protein contains a characteristic region scientists have termed a "zinc finger" because it loops around a molecule of zinc. Zinc fingers give proteins a specific shape that allows them to bind with DNA and regulate whether or not the DNA sends out instructions for protein synthesis.

"This new work underscores the use of genomic approaches to identifying genes involved in development of leukemia in patients not predisposed by heredity to get cancer," says NCHGR acting director Dr. Michael Gottesman, who also studies cancer genetics.

According to the report, the findings suggest that the breakage in chromosome 11 during translocation disrupts the function of the human *trx* gene, making it unable to produce a normal protein. Genes the protein might act upon have been found to be active in white blood cells. Without the *trx* protein to regulate the function of such a gene, blood cells could grow out of control, resulting in leukemia. Further analysis of the 11q23 region "should clarify mechanisms of gene control and deregulation in chromosome 11q23-associated leukemias," the report says. □



Dr. Diane Blackmore Forsythe, a clinical veterinarian in NIEHS' Comparative Medicine Branch, has been appointed acting chief of the branch. She will manage a program for experimental animal procurement, housing and utilization for NIEHS and advise institute scientists on appropriate animal models. She was recently certified as a diplomate of the American College of Laboratory Animal Medicine. Forsythe, who received her D.V.M. from Cornell University in 1984, joined the CMB in 1988.

The NIH Record

Published biweekly at Bethesda, Md., by the Editorial Operations Branch, Division of Public Information, for the information of employees of the National Institutes of Health, Department of Health and Human Services, and circulated to nonemployees by subscription only through the Government Printing Office. The content is reprintable without permission. Pictures may be available on request. Use of funds for printing this periodical has been approved by the director of the Office of Management and Budget through September 30, 1993.

NIH Record Office
Bldg. 31, Room 2B-03
Phone 496-2125
Fax 402-1485

Editor
Richard McManus

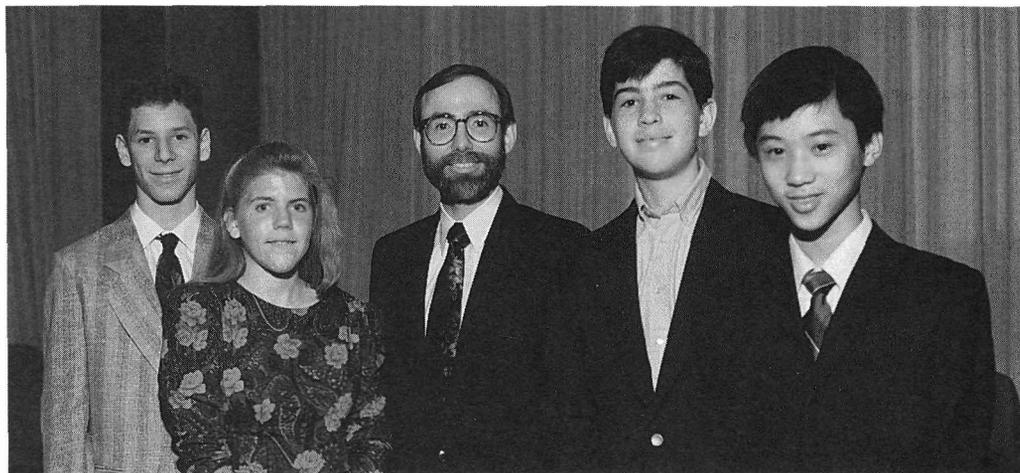
Assistant Editor
Anne Barber

Staff Writer
Carla Garnett

Editorial Assistant
Marilyn Berman

Correspondents:
CC, Sue Kendall
DCRT, Anne P. Enright
DRG, N. Sue Meadows
FIC, Jim Bryant
NCI, Patricia A. Newman
NCHGR, Leslie Fink
NCNR, June Wyman
NCRR, Polly Onderak
NEI, Linda Huss
NHLBI, Louise Williams
NIA, Vicky Cahan
NIAAA, Ann M. Bradley
NIAID, James Hadley
NIAMS, Amy Iadarola
NICHD, Carol Florance
NIDA, Karen Rogich
NIDCD, Gail Blatt
NIDDK, Eileen Corrigan
NIDR, Mary Daum
NIEHS, Hugh J. Lee
NIGMS, Wanda Wardell
NIMH, Marilyn Weeks
NINDS, Carol Rowan

The NIH Record reserves the right to make corrections, changes, or deletions in submitted copy in conformity with the policies of the paper and HHS.



Four students from Montgomery County Public Schools were recognized by the NIH Office of Education for their accomplishments in original research at the Montgomery County Science Fair. Shown here with Dr. Michael Fordis (c), OE director, are (from l) Ryan Katz, Wootton High School, who was awarded a summer internship at NIH; Stacy Killpack, Damascus High School, \$50 Savings Bond recipient; Daniel Rosenbaum, Walt Whitman High School, \$50 Savings Bond recipient; and Davy Yuan, Wootton High School, \$100 Savings Bond recipient.

Researchers Write Primer on Challenges of Minority Recruitment

By James Hadley

One of the greatest challenges facing AIDS researchers today, besides trying to find viable treatments and a cure for the disease, is the recruitment and retention of minority patients for clinical trials.

With the epidemic moving swiftly into the minority community, inclusion of these patients in clinical trials is particularly urgent.

Two NIAID-supported investigators, Drs. Wafaa El-Sadr and Linnea Capps, both of Harlem Hospital and Columbia University College of Physicians and Surgeons, have published what is considered by experts to be a primer on "The Challenge of Minority Recruitment in Clinical Trials for AIDS" in the *Journal of the American Medical Association* (Vol. 267, No. 7).

The article focuses on the influence of socioeconomic factors responsible for the difficulty in getting African Americans who are poor and live in urban areas to participate in clinical trials for HIV infection. The authors acknowledge that some of these reasons may apply to other racial groups as well.

"Clearly Drs. El-Sadr and Capps have their pulse on the community they serve in New York City," says Dr. George W. Counts, NIAID assistant director for minority affairs. "The article provides a model for a successful recruitment effort that is inclusive, rather than exclusive."

Ideally a researcher's goal is to achieve minority representation in clinical trials that mirrors their representation in the community, Counts explains. Another goal is to ensure equal opportunity in trials participation for all HIV-infected persons, he adds.

"This new model," says El-Sadr, "must reflect the special needs of these communities and should recognize and meet head-on the historical distrust of clinical trials—particularly among African Americans—and the need for extensive educational and social support services."

As the next century approaches, the face of AIDS is changing. Statistics show that AIDS is becoming less and less a disease of white, gay men in the United States. Minorities now constitute 47 percent of the 230,179 cases of AIDS reported.

Minorities are disproportionately represented among those with AIDS. While African Americans comprise 12 percent of the U.S. population, they are 29.5 percent of all adult AIDS cases. Also, Hispanics comprise 9 percent of the U.S. population and 16.6 percent of all adult AIDS cases.

Yet the number of minority patients in clinical trials for HIV infection has remained disproportionately small. This underrepresentation is apparent in the literature reporting landmark studies on treatments against AIDS and its complications. Also, some



Dr. Wafaa El-Sadr is coauthor of a primer on recruiting minorities into clinical trials for AIDS.

studies show no racial breakdown of participants.

In the *JAMA* article, El-Sadr and Capps say successful recruitment requires an extensive educational effort. The authors emphasize that an explanation of basic research terminology is essential. A prospective participant must understand the meaning of a clinical trial, random sampling, the nature of blinding, the concept of a placebo and the responsibilities of the patient and the provider.

Only after a patient has a full understanding of these issues should the specific protocol be discussed. The authors believe that many of the widely available educational materials lack cultural sensitivity and consideration of socioeconomic factors or of low literacy levels.

"This is a time-consuming process for researchers and staff," they caution. "It requires educational skills, patience and the building of trust."

Researchers must accept that successful recruitment is more than supplying the study drug, they explain. It may mean providing a hot meal or meal vouchers, meeting transportation needs or providing child care.

Moreover, additional staff may have to be hired to augment the clinic staff. A social worker and outreach worker may have to help patients with the social needs that often impede their ability to participate in clinical trials.

Patients may be homeless, active drug users or women with children. They may lack resources for transportation, food or nutritional supplements. Social workers should monitor the support networks of patients and provide information on housing, substance abuse programs and other services. Outreach workers should track down patients and assist them in making protocol-related visits.

For example, at Harlem AIDS Treatment Group—one of NIAID's Terry Beinr Commu-

nity Programs for Clinical Research on AIDS centers—innovative services complement research protocols. A videotape and pamphlets address the concerns of the African-American patient about clinical trials. Peer groups for clinical trial participants encourage patients to follow the research protocol and provide personal testimonies for others who may be interested in joining the trial. The services of a social worker and outreach worker are available. A van provides transportation to the clinic.

Research participants are incorporated into a system that attempts to meet multiple personal needs. Failure to fulfill these needs, warn El-Sadr and Capps, will doom well-meaning attempts to recruit and retain minorities in clinical trials.

"The compelling scientific, ethical and social reasons for inclusion of minorities in clinical trials justify the necessary efforts to accomplish this important goal," the authors conclude. □

Tech Transfer Forum, Oct. 29-30

The NIH Office of Technology Transfer will sponsor a forum titled, "Designing New Therapeutic Strategies for Cancer and AIDS," on Oct. 29-30 in Masur Auditorium, Bldg. 10.

After an opening session (P.S. Chen, B. Healy, B.A. Chabner, L. Liotta), there will be sessions on "Drug discovery and development strategies" (M. Grever, M.I. Johnston, M.M. Gottesman, J.N. Weinstein), "Structure-based drug design" (M. Cassman, I. Kuntz, A. Wlodawer, T. Steitz), "Biological therapy" (A.S. Rabson, K.L. Longo, T.W. Waldmann, R. Redfield), "Drug delivery strategies" (G. Guroff, R.L. Dedrick, S. Rybak, R. Langer) and "Gene therapy" (B. Moss, A.W. Nienhuis, S.A. Rosenberg, W.A. Haseltine). There will also be special lectures on "Angiogenesis as a target for therapy" (J. Folkman), "An FDA perspective on development of new therapies" (K. Zoon), and "The future of AIDS therapy" (D.F. Hoth). At 7:30 p.m. on Oct. 29 there will be a roundtable discussion on "Clinical trials and technology transfer" (R.G. Adler, R. Yarchoan, M.A. Guerra, T.D. Mays, J.A. Kalkstein).

In addition to its scientific content, the forum is intended to facilitate research collaborations between government scientists and industry, pursuant to the Federal Technology Transfer Act of 1986. An updated technology transfer directory (including policy guidelines and model agreements, current CRADAs, and PHS inventions available for licensing) will be distributed at the forum. For more information call Carolyn Craig, 496-7736. □

Peace Corps Vets To Meet

Former Peace Corps volunteers are invited to lunch at the Bethesda Room in the Bldg. 10 Eatery on Wednesday, Nov. 18 at 11 a.m. Guests should arrive promptly since there is a second luncheon seating at 12:30 p.m. The cost of lunch is \$6.95 and includes an entree, salad bar, dessert, and beverage. Call Kathleen Crosson, NCI, 496-6792, or Becky Parks, CC, 496-4733, ext. 706, if you plan to attend. □

ROSENBERG

(Continued from Page 1)

"There's no place in the world like NIH," enthuses Rosenberg, both in person and in the pages of his memoir. "There are some problems here, but when it comes to marrying science and medicine, no where else in the world comes close. The advantages far outweigh the problems."

Rosenberg got the idea of writing a book several years ago, but was reluctant to take any time away from his patients and research to pursue such a project. At the urging of publisher G.P. Putnam's Sons, he agreed to a book, but only with the aid of a coauthor.

"I decided I needed some help," he remembers. "I was determined not to take a minute away from my lab work."

Putnam's provided him with a list of a dozen writers; Rosenberg eventually settled on John M. Barry, author of *The Ambition and the Power: A True Story of Washington*, which is



Dr. Steven A. Rosenberg stands in front of a wall in his office on which hang portraits of most of the research fellows who have worked with him in the past 20 years at NIH.

about former Speaker of the House Jim Wright.

"I liked that book very much," said Rosenberg. "I deliberately didn't want a science writer. I wanted to provide the scientific explanations myself. Barry turned out to be the right person. It was a superb partnership."

Working late at night, the two wrote first drafts of the book. Rosenberg estimates that he rewrote each chapter five times. "I revised everything. The final word on the book was my responsibility."

Recalling his pleasure in reading *The Double Helix* by Watson and Crick, Rosenberg set out to write the kind of book he would enjoy reading.

"Scientific research is, after all, a mystery story," he explains. "You're following clues, tracking down a killer. The book attempts to explain to the nonscientist how medical research is conducted. People need to understand how NIH works, and about the need for animals in research, the need for public funding for research, and the scientific and ethical issues involved."

"I want people to understand how scientists



Rosenberg (standing, c) and his gene therapy team

gather information," he continued. "Most people are eager for the benefits of research, but don't understand how we got to where we are today."

The book is perhaps brutally frank about how often scientific hypotheses and experiments fail; even his mother urged Rosenberg to deemphasize the negative results in his book.

"A lot of science is failure," he concedes. "Seventy-six patients in a row died before our first success. But good scientists are energized by failure, not defeated."

"Medical research," he declares, "is not an intellectual exercise or a search for ultimate truth. It's an attempt to solve desperate human problems of disease."

Rosenberg, who knew he wanted to be a scientist while still a teenager, sees science as "the most humanizing of the human endeavors, the best hope we have to enable everyone to live out their human potential."

The book listens in as Rosenberg sizes up the character of both patients and employees, reveling in this one's strengths and recognizing that one's weaknesses.

"I wanted to be honest," said Rosenberg, reemphasizing that science is a "very human activity. I haven't said anything in the book that I wouldn't say to someone's face. There's no room for ceremony in science—everybody criticizes everybody else in the search for the right answers."

The virtue of hope emerges as most dear to Rosenberg and his colleagues. "It's important to provide hope for people who don't have any hope," he said. "Over the years, many, many patients have told me that the worst thing about serious illness is the loss of hope. It's worse even than the disease."

Rosenberg has hope for a succession of treatments as the book proceeds, from infusions of pig lymphocytes in 1976, to low-dose interleukin-2 trials in 1983, to the use of TIL (tumor-infiltrating lymphocytes), LAK (lymphokine activated killer cells) and TNF (tumor necrosis factor) in clinical trials, to the first introduction of a foreign gene in a human in 1989. As the book ends, Rosenberg envisions treating 100 patients with gene therapy by the end of 1994.

While he admits there is, as yet, no cure, Rosenberg believes he's got a foot in the door of a disease that claims some 500,000 American lives each year. "We have shown that it is possible to use strictly immunologic procedures to make cancer go away. We have added a fourth treatment modality (to surgery, chemotherapy and radiation) and are struggling to improve it. You have to remember that we are very early in (immunotherapy's) development. We're trying to use as much modern science as we can to improve our strategies. Gene therapy is a very important new tool. We are no longer limited by the kind of cells and physiologic processes that nature has provided the cancer patient."

Rosenberg says it is much too early to assess the efficacy of new therapies involving gene-modified tumor cells—components of the so-called "cancer vaccine." "But we do know that you can safely apply these gene manipulations to patients," he maintains. "Gene therapy can potentially change the whole face of medicine in the next century."

Driving his multimillion dollar research effort is the idea that "maybe the next patient will be the person who teaches us how to (treat cancer) better."

Rosenberg is back in the lab full-time now, with no more nontechnical book plans for the future. "I think there have only been about 10 days in the past 20 years when I wasn't here (in his Clinical Center laboratory or ward) at some point," he says. "The toughest thing about (his career) is leaving the hospital. Basically you never leave it. It's always with you."

To understand that degree of dedication, read the book. □

Healthy Volunteers Needed

The Neuropsychiatric Research Hospital of NIMH needs healthy volunteers between the ages of 18 and 45, on no medications, to participate in various studies. These include psychological testing, eye-tracking studies, PET scan studies, MRI scan studies, and/or serum and CSF studies. Subjects will be paid. For more information call (202) 373-6109. □

Brain Chemical May Hold Clues to Alzheimer's Treatment

Scientists have discovered a critical link between the brain chemical acetylcholine and the body's ability to metabolize a protein that causes harmful deposits in the brains of people with Alzheimer's disease.

The research, which was supported by NIMH and NIA, suggests that treatment using drugs that act like acetylcholine can slow the buildup of the protein amyloid and perhaps delay the onset of this devastating brain condition.

An estimated 4 million Americans are afflicted with Alzheimer's disease, a disorder that usually begins after age 65. It causes memory loss and leads to death after 6 to 10 years of steady mental decline. Currently, there are no treatments for the disease.

In the Oct. 9 issue of *Science*, authors Roger M. Nitsch, Barbara E. Slack, Richard J. Wurtman and John H. Growden, all with the Massachusetts Institute of Technology, report that the neurotransmitter acetylcholine plays a major role in stimulating breakdown of amyloid precursor protein (APP).

Nearly every cell in the body produces APP, which is metabolized by several alternative pathways, said Nitsch. One way produces harmful fragments called beta-A4, which form an insoluble protein called amyloid. Buildup of this protein is one of the major abnormalities found in the brains of people with Alzheimer's disease. A second way APP is metabolized causes the formation of harmless fragments, which cannot become amyloid.

Wurtman and his colleagues already knew that healthy brains with few amyloid deposits have normal levels of acetylcholine. In addition, it had been shown that people with Alzheimer's disease have acetylcholine deficiency, which eventually leads to memory loss. The research team hypothesized that acetylcholine stimulated the safe breakdown of APP—and that acetylcholine deficiency caused the undesirable APP metabolism to take place.

To test their theory, the team cultured human cells that each contained both APP and one of four receptors for the neurotransmitter acetylcholine. They found that when cells containing the m1 or the m3 receptor were stimulated by carbachol, a synthetic drug that resembles acetylcholine, they broke down APP by the harmless pathway three to five times more rapidly. This indicates that the formation of the harmful fragments is decreased simultaneously.

"Our research showed, for the first time, that neurotransmission and APP metabolism are related," said Nitsch.

Wurtman said the research team believes the neurochemical abnormalities in Alzheimer's disease are related in this way: Certain acetylcholine-releasing neurons are damaged by the disease. This leads to a reduction in acetylcholine release and also reduces the breakdown of APP into harmless fragments, thereby increasing the formation of fragments that can make

up amyloid.

Dr. Frederick Goodwin, NIMH director, said the research results hold promise for people with Alzheimer's disease. "With this finding, we see opportunities for new drugs that might prevent the buildup of amyloid in the brain," he said. "This could help relieve the memory loss suffered by people with Alzheimer's disease—and possibly even delay onset of the disorder."

If a diagnostic test can be developed to identify people at risk for Alzheimer's disease, preventive treatment approaches suggested by this research might include designing drugs that are similar to acetylcholine and can enhance normal APP processing. Another strategy would involve the use of drugs that inhibit metabolism of APP by the pathway that results in buildup of amyloid.

"Alzheimer's disease has been conceptualized in two ways—as an aberration of amyloid protein metabolism and as a disease of neurotransmitter deficiency," said Wurtman. "That meant we would have to treat the disease in two entirely different ways. Now there's a connection, and we can hope that a very specific kind of drug—one that corrects the acetylcholine deficiency and suppresses the production of amyloid—might be effective." □



NIAID's Dr. John E. Bennett delivered the 21st annual Maxwell Finland Lecture at the recent Infectious Disease Society of America meeting in Anaheim. One of the nation's leading experts on systemic fungal infections, he is chief of the clinical mycology section in the Laboratory of Clinical Investigation. His lecture, "Cryptococcus: The Sugar-Coated Killer," focused on Cryptococcus neoformans, a fungus that infects more than 5,000 Americans each year and is fatal unless treated. Bennett and his colleagues have created a vaccine, now under trial to determine whether it prevents cryptococcosis in patients infected with the human immunodeficiency virus (HIV-1).

Two NIH'ers Elected to AAAS

Dr. Ira H. Pastan, chief of the Laboratory of Molecular Biology, NCI, and Dr. Kiyoshi Mizuuchi, chief of the genetic mechanism section, Laboratory of Molecular Biology, NIDDK, were recently elected to the American Academy of Arts and Sciences in recognition of their contributions to biological science.

Pastan has conducted research on mechanisms of hormone action, the control of gene transcription in bacteria by cyclic AMP, and the mechanism of cancer cell transformation. He is recognized for his work in creating new anticancer drugs by fusing modified forms of *Pseudomonas* exotoxin to growth factors and antibodies. The recombinant toxins selectively kill cells with specific proteins on their surfaces. Two of these chimeric toxins are now entering clinical trials as AIDS and cancer therapies. He has also conducted substantial research on the basis of multidrug resistance in human cancer.

Mizuuchi's research has focused on DNA transposition, the process by which well-defined DNA segments move from one place in the chromosome to another, or from one cell to another. This process is responsible for much of the spread of antibiotic resistance among bacteria. Mizuuchi has extended this work to study the way that retroviruses such as HIV integrate into the chromosomes of infected cells, a process that is very similar to bacterial transposition. His research has led directly to a method for rapidly screening drugs for their effectiveness against the integration step of the HIV life cycle.

The academy, founded in 1780 by John Adams and other early leaders of the United States, gathers the country's leading figures from academia, government, business, and the arts to exchange ideas and promote knowledge for the public interest. □

Stetten Symposium Set, Oct. 28

"From Basic Research to Biotechnology," the NIGMS DeWitt Stetten, Jr. Symposium, will be held in Masur Auditorium at 2:30 p.m. on Wednesday, Oct. 28. Nobel laureate Dr. Thomas Cech will speak on "RNA as an Enzyme: From Chemistry to Biotechnology"; Dr. Peter Schultz will discuss "Catalytic Antibodies"; and Dr. James Bailey will describe "Cellular Biotechnology: Engineering Metabolism for Enhanced Productivity and New Products." For more information call 496-7301.

Allergy Study Needs Vols

FDA/NIAID seeks volunteers who are allergic to latex/rubber, dust, mold, and peanuts to participate in a study involving blood donation and allergy skin testing. Participants will be paid. Send written requests to Jackie Matthews, Bldg. 29, Rm. 201. □

CFC KICKOFF
(Continued from Page 1)

surely hang separately," he called for a common effort on the part of all NIH'ers to participate in the annual charity effort.

"CFC could even stand for the Combined Future Campaign," he said. "Our CFC contributions will help determine that future, the future we share together."

Also speaking was Cpl. Edward Landicho of the NIH Police, who was recently honored at the International Law Enforcement Olympics with five medals. With the hardware draped around his neck, he said, "This shows that NIH can compete with the best in whatever we do," including raising money for charity. He offered a recipe for CFC success: "Be a team. Work together. Support one another. It worked for me and my teammates and it can work for you." He then raised a barbell over his head as his fellow police Olympians spoke this year's CFC slogan—"All We Need Is You."

Following the speeches, health enthusiasts gathered on Center Dr. in front of Bldg. 1 for the traditional 5,000-meter run and walk, sponsored by Health's Angels Running Club. Diggs fired the starter's pistol to begin the race, results of which were:

| | Overall Place | Time |
|----------------------------|---------------|-------|
| Men, 39 and under | | |
| Richard Crowley | 1 | 16:40 |
| Dana Ziegler | 2 | 16:52 |
| Bob Kneller | 3 | 17:23 |
| Men, 40 and over | | |
| John Kusek | 6 | 18:30 |
| Mark Buller | 13 | 19:33 |
| Bill Elzinga | 15 | 19:47 |
| Women, 39 and under | | |
| Lauren Flores | 22 | 20:37 |
| Carolyn Bouma | 23 | 20:43 |
| Patricia Day | 24 | 21:15 |
| Women, 40 and over | | |
| Alison Wichman | 21 | 20:29 |
| Georgina Miller | 35 | 22:51 |
| Pat Earl | 47 | 23:59 |



Participating in the traditional campus walk are parents and children affiliated with POPI—Parents of Preschoolers, Inc., a CFC organization active on the NIH campus. There are about 300 more organizations listed in the CFC brochure this year than last year, reflecting the continuing needs of the community for neighborly help.

NOBEL LAUREATES ARE LONGTIME NIH GRANTEES

(Continued from Page 1)
action.

They also discovered another class of enzymes called phosphatases, which deactivate these proteins. Together, these two classes of enzymes form the basic mechanism whereby cell activities are turned on and off. Imperfections in this control mechanism are an underlying cause of many disease processes.

The significance of their work was not immediately known, not even to the scientists themselves. But over several decades, other scientists began to expand on the cell regulation work of Krebs and Fischer. Today, their discovery is considered a key towards understanding the connection between cell activities and various diseases and in developing drugs to combat an on-off regulatory system that has gone haywire.

"The Nobel Prize is not only a great personal honor for Krebs and Fischer, but an honor for the NIH," said NIDDK director Dr. Phillip Gorden. "This award clearly demonstrates the benefit of basic biomedical research and the potential it has for the conquest of a host of diseases that afflict Americans and people around the world."

Fueling the researchers' efforts was funding from the NIDDK, which has supported Krebs continuously since 1951 (total, \$3,554,751) and Fischer continuously since 1956 (total, \$4,466,147). Their long journey began with a few thousand dollars for each scientist in the late 1950's. NIGMS also supported the researchers in the early part of their careers. Both scientists have also served on NIH review groups: Fischer on the physiological chemistry review committee, 1984-1987; Krebs was on a diabetes committee in 1979-1983.

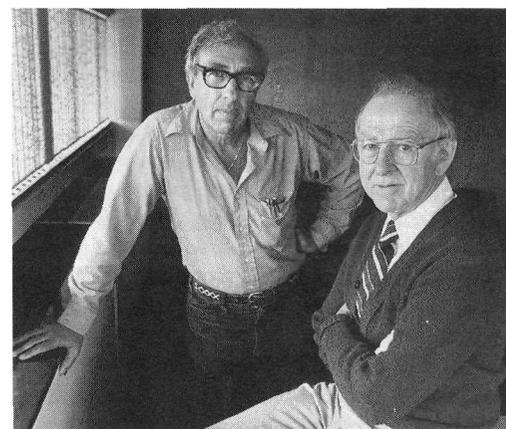
Krebs said at a news conference that it would be harder for young scientists to receive the same type of support for basic research today because grants are more geared towards applied research. Krebs feels that this is unfortunate because an understanding of basic research is

NIH Charities in CFC

There are at least three NIH-related interests represented in this year's Combined Federal Campaign. Camp Fantastic/Special Love (#2055) provides young cancer patients with stimulating programs and recreational opportunities. Emergency financial assistance is offered. Cancer families are provided with a network of caring through shared experiences.

The Children's Inn at NIH (#2443) is a national resource providing supportive residence and services to pediatric patients and families undergoing treatment at NIH.

Friends of the Clinical Center (#2134) helps patients and their families with financial support to ease pain and crisis of illness during hospitalization at NIH. When you pledge CFC this year, think of NIH.



Drs. Edmond Fischer (l) and Edwin Krebs

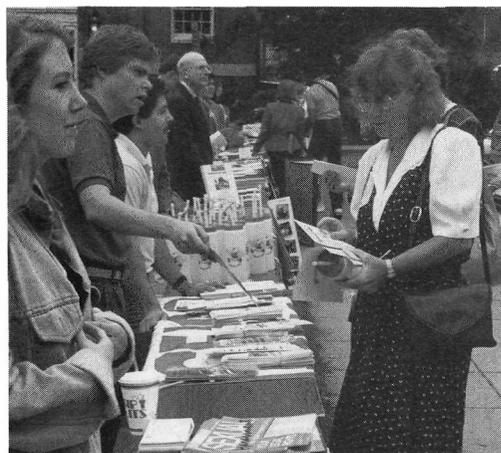
fundamental in finding a way to combat disease.

The Nobel Prize by no means marks an end to the scientists' research efforts. Both still head active research teams. Krebs, 74, is exploring hormonal regulation, which is important for a better understanding of diabetes. Fischer, 72, studies cell transformation, which has important implications for cancer.

Their discoveries have not only provided insights into the mechanisms of cell regulation but have also opened up new fields that are beginning to shed light on the control of various diseases. The booming field of biotechnology, which hinges on a basic understanding of cell regulation to produce genetically engineered drugs, owes part of its growth to the legacy of Krebs and Fischer.

NIH funding has underwritten the work of numerous Nobel Prize-winning researchers over the years. Since 1956, the NIDDK has supported the work of 17 Nobel laureates.

The award was initiated by Alfred Nobel, the inventor of dynamite. Krebs and Fischer will receive their prize on Dec. 10 in Stockholm, Sweden, at a ceremony marking the anniversary of Nobel's death.—Mark T. Sampson □



NIH'ers browse among the tables set up in front of Bldg. 1 by CFC-eligible organizations, many of which offered souvenirs.

Comprehensive Genome Map Published by NCHGR Grantees

Human Genome Project researchers have compiled the most comprehensive map so far of the human genome. The new map, a type known as a genetic linkage map, contains 1,416 molecular markers, covers over 90 percent of the genome, and represents the most up-to-date publication to contain all the available information on genetic linkage mapping depicted in the same format. The map will be a starting point for the continued collection and placement of new and better-quality DNA markers that will allow researchers to tie together gene-finding information from the several different types of chromosome maps used in gene hunts.

Appearing in the Oct. 2 issue of *Science*, the map is a product of the National Center for Human Genome Research's effort to coordinate gene mapping activities into a unified project and to support the development of better, more useful chromosome maps.

"The major difference between previously published maps and those presented here," the article says, "is the informativeness and type of marker now being used." The authors predict these new markers, made of small numbers of repeating DNA bases, "will become the dominant type of markers on the map."

A result of the NCHGR and the Centre d'Etude du Polymorphisme Humain Collaborative Mapping Group, the map was collated and edited by Washington University (St. Louis) geneticist Dr. Helen Donis-Keller. More than 70 laboratories have contributed to the map, which includes markers from CEPH's vast collection of DNA samples and family tree information that has proven invaluable to researchers worldwide who are assigning markers to chromosomes.

"In order to unify a large amount of genotypic data currently available from the CEPH database and collaborating laboratories," the article says, "members of the genetic mapping community have joined together to construct a genetic linkage map of the human genome, which is presented here in a common format." The map should provide a useful tool for mapping disease genes, the report says, even when family tree information is limited.

Genetic linkage maps are one kind of chromosome map being constructed under the Human Genome Project and are used in the first steps of a gene hunt. By correlating the inheritance of markers with the appearance of physical traits in large numbers of relatives, scientists can estimate which chromosome a gene resides on. Statistical calculations based on inheritance information can also reveal the distance between markers.

The first human chromosome maps, called cytogenetic maps, were developed in the 1950's using staining techniques that showed light and dark banding patterns on chromosomes. These bands served as the only genetic markers available until 20 years later, when scientists discovered differences between individuals in

the places where their DNA is snipped by DNA-cutting enzymes. These differences resulted in DNA pieces of varying lengths, which often differed from person to person, and were eventually called RFLPs or "riflips." Riflips quickly became the state of the art in genetic mapping.

Although they contributed greatly to advances in gene mapping, riflips had some important limitations. They do not appear to be distributed evenly throughout the genome, and they are cumbersome to make and use in the laboratory. Also, riflip patterns often do not differ frequently enough from one person to the next, a characteristic known as "polymorphism," to allow scientists to track them through families. Markers that are seldom polymorphic are not "informative" to researchers, which makes it difficult to link a physical trait to the inheritance of that marker.

As little as 5 years ago, genetic linkage maps consisted of only a few hundred markers. Most of these were riflips and only a few percent of them were of high enough quality to be useful in tracking genes in large populations. More recently, researchers discovered small numbers of repeating DNA sequences, called microsatellites, scattered throughout the genome. The number of times these sequences repeat is frequently different between individuals, a feature that makes microsatellites easily traceable and highly informative markers. And

World Congress on Tuberculosis To Meet in Bethesda, Nov. 16-19

A World Congress on Tuberculosis will be held Nov. 16-19, in Bethesda. The meeting will provide an opportunity for an international group of scientists, physicians and health care workers to discuss prevention and control of tuberculosis, which has re-emerged as a major problem in the United States and continues as an important global health threat.

One-third of the world's population is infected with the TB organism, including 10 million to 15 million Americans. With an estimated 8 million new TB cases and nearly 3 million deaths each year worldwide, TB is the leading cause of death from any single infectious disease. The containment of TB in the U.S. was well within reach until a few years ago. Since 1985, however, the number of TB cases in the U.S. has increased by more than 18 percent in 1991 to more than 26,000, with 2,000 deaths annually.

Scheduled speakers include HHS secretary Dr. Louis W. Sullivan, HHS assistant secretary for health Dr. James Mason, NIAID director Dr. Anthony S. Fauci, and other leading representatives from international organizations.

An infectious disease, TB is caused by prolonged exposure to the bacterium *Mycobacterium tuberculosis* or *M. africanum*. The bacteria can be transported in droplets when a person with active TB coughs or sneezes,

because microsatellites are actual DNA sequences, they can be used as anchors to connect the genetic linkage map with maps made of DNA clones, called physical maps, as well as with the band patterns on cytogenetic maps.

"The popularity of microsatellites over RFLPs is due to their high degree of informativeness, convenience of assay by PCR [the DNA-amplifying method known as polymerase chain reaction], relatively even distribution throughout the genome, and availability," the article says. Microsatellite information can be obtained from computer databases by almost any researcher.

Through statistical calculations, the authors estimated the distances between the markers on the new map. The closer the markers are, the better "picture" scientists can get of the region they are studying. For most chromosomes, markers on the new map are spaced about 5 centimorgans apart. One centimorgan equals approximately 1 million bases.

With the addition of more microsatellite markers to the genetic map, information from linkage maps and clone-based physical maps will converge, the authors conclude. "It is anticipated full integration of genetic, cytogenetic and physical mapping information will be possible, thereby providing a new 'view' of the [human] genome upon which to base future biological studies." □

allowing invasion of the air sacs of the lungs and spread to lymph nodes and other organs of susceptible individuals.

In the developed world, the use of antibiotics had brought TB under control until the mid-1980's. Among the causes for the resurgence of TB are the epidemics of HIV infection and AIDS. HIV-infected people are especially susceptible to TB because they have weakened immune systems.

Other factors contributing to TB's re-emergence include that it is a contagious disease and that antibiotic treatment for the disease must include a number of drugs taken for a period from 6 months to a year, which makes treatment compliance difficult. The lack of compliance leads to the emergence of new forms of the bacteria that are resistant to one or more antibiotics.

The congress will focus on the management and confinement of TB globally, through basic and applied research in the diagnosis, treatment and prevention of TB, as well as behavioral and operational research.

Organizers of the congress include the Fogarty International Center, NIAID, NHLBI, the Office of AIDS Research and the Office of Minority Programs of NIH; and others.

For more information, contact the International Studies Branch, Fogarty International Center, Bldg. 31, Rm. B2C32. □

ANNIVERSARY

(Continued from Page 1)

research training activities at minority institutions.

Cutting-Edge Research

NIGMS consists of five program branches: Cellular and Molecular Basis of Disease, Genetics, Pharmacological Sciences, Biophysics and Physiological Sciences, and Minority Opportunities in Research (which includes MARC and MBRS), all of which support both research and research training. NIGMS has no



"NIGMS supports basic research in order to broaden the base of biomedical knowledge and to produce answers to general questions. These answers are, in turn, critical to the construction of rational and systematic approaches to the problems of disease." Dr. Ruth L. Kirschstein, (NIGMS director since 1974)

laboratories on the NIH campus. With the exception of a small intramural training program, the research and research training activities supported by the institute take place at universities, medical schools, hospitals, and research institutions throughout the country.

Basic untargeted research, such as that supported by NIGMS, often results in the discovery of fundamental principles that shape the way scientists approach the problems of disease. One indication of the significance of this research is the fact that over half of the NIH-supported Nobel Prize winners have received grants from NIGMS.

"Science has made amazing strides in the past 30 years," notes NIGMS director Dr. Ruth Kirschstein, "but, today, the need for a basic research institute is just as great as—or perhaps greater than—it was in 1962, because much still needs to be learned about how basic biological systems work before we can understand how to correct many disorders."

For instance, in 1962, there was no way the founders of NIGMS could have predicted the development of recombinant DNA technology. Scientists knew that studies of DNA structure and function had the potential to yield information of critical importance, but no one knew

that these studies would lead to a day when a single gene could be separated, purified, synthesized, inserted into the DNA of bacterial cells, and the protein for which it codes produced in all the progeny of those bacteria.

The year NIGMS became an institute—1962—was less than 10 years after the publication of the critical paper that described the structure of DNA. Scientists were just beginning to learn how the DNA bases code for amino acids.

In the first 10 years that NIGMS was an institute, its grantees discovered restriction enzymes, which made it possible to cut DNA at specific places. Other grantees were instrumental in the discovery of ligase, which made it possible to "stick together" spliced pieces of DNA. These were the tools that permitted the development of recombinant DNA technology, which—very simply put—has revolutionized biomedical science. Not only are scientists today able to ask questions undreamed of before the technology was developed, but also many direct clinical benefits, such as gene therapy for some diseases, are beginning to be realized.

By the 1980's, recombinant DNA technology had formed the basis of the rapidly growing biotechnology industry, and the first drugs produced by these techniques, including human insulin and human growth hormone, had appeared on the market. Ten years later, 11 medicines that were made through biotechnology were available to physicians, and more than 100 additional "biotech" drugs and vaccines were in various stages of the testing and approval process.

By laying the foundations for this important new industry, NIGMS-supported basic research



"Each of the categorical institutes had been established as a result of the desires of members of Congress to attack specific illnesses; the establishment of the Division of General Medical Sciences [later to become NIGMS] was based on a professional judgment of the administrators of the NIH and their advisors that there were gaps between the research programs of various institutes which required the new entity." Dr. G. Halsey Hunt (DGMS director 1958-1962)



"I saw ... providing research support and graduate training predominantly in basic sciences as a major support element to the other institutes of NIH." Dr. Frederick L. Stone (NIGMS director 1964-1970)

has resulted in direct economic benefits. Many nonbiomedical industries, such as agriculture and food processing, have also benefitted from the application of biotechnology, and the potential for future applications is tremendous.

Another important area in which NIGMS-supported research has had a critical impact is the mapping of human genes, particularly those genes that cause disease. In the past 10 years, researchers have located the genes for many serious genetic disorders. One method for mapping the location of specific genes on chromosomes is restriction fragment length polymorphism technology, which was developed by NIGMS grantees. Once a gene known to cause a disorder has been located and characterized, researchers can better diagnose the disorder and begin to develop new treatments for it.

Genetics and Cell Biology

There is often cross-fertilization in the research supported by NIGMS branches. A particularly striking example occurs in the field of cell cycle research. Although geneticists and cell biologists originally approached cell cycle studies from different directions, their work has converged and is now shedding light on processes of normal and abnormal development and growth, including cancer.

Clinical benefits are now beginning to result from the intersection of years of research in basic cell biology with studies of cancer biology, immunology, developmental biology, and hematology. For decades, cell biologists studied the fundamental mechanisms of cell adhesion. It was hoped that this work would shed light on such questions as why cells either stick together too well—causing the chronic inflammation seen in diseases like arthritis—or don't stick together well enough—a process that enables cancer cells to slip away from the primary site and metastasize. But first, the scientists needed

to build a body of knowledge by isolating and carefully characterizing the molecular mechanisms involved.

Now, this research has advanced to the drug development stage. One of the first drugs, which enhances cell adhesion and thus is designed to speed wound healing, is in the approval process. Other drugs are being developed to treat shock and to prevent bits of broken-up blood clots from causing further clots. Eventually, biotech companies may be able to develop drugs to prevent the metastasis of cancer cells.

Another exciting discovery, made by NIGMS-supported and other developmental biologists in the past decade, has been the identification of homeoboxes, which are highly conserved DNA sequences involved in the development of organs and other body structures. Homeoboxes have been characterized extensively in fruit flies, since mutations in homeobox-containing genes of these organisms can be easily studied.



"Studies on basic genetic mechanisms were in full swing, and I vividly recall the time at the appropriation hearings when Dr. Shannon and I [explained] the significance of DNA and the genetic code to members of the committee." Dr. Clinton C. Powell (DGMS/NIGMS director 1962-1964)

Although homeoboxes have been identified in other species, it has only recently been shown that they affect the development of body structures in these species as well.

DNA and RNA

Over the years, basic researchers have uncovered many surprises about DNA and RNA. For instance, they discovered that the genes of higher organisms contain large sections of DNA, called introns, that do not appear to have a protein-coding function. They have also found that DNA contains segments called transposable elements, which spontaneously move from one location to another. Recently, a study showed for the first time that movement

of a transposable element is involved in a genetic disease, in this case, hemophilia.

Scientists are also finding that RNA is much more complex than they previously thought. In the early 1980's, NIGMS grantees (who later received the Nobel Prize for this work) showed that certain RNA molecules possess catalytic activity—that is, they can perform the enzyme-like function of speeding up chemical reactions. This unexpected finding has revolutionized research on RNA. Researchers are now working with these catalytic RNA molecules, called ribozymes, to see if they can be engineered to perform various useful functions, including the destruction of harmful viruses. Initial attempts to create "designer" ribozymes have been encouraging.

Studies of RNA may also yield other innovations that could prove useful to the pharmaceutical and biotechnology industries. One example of this is "antisense" RNA. This form of RNA is made from the strand of the DNA double helix that is not normally transcribed into the RNA that codes for protein. Antisense RNA can block the transcription of the complementary coding sequence, raising the possibility of using antisense RNA's to inhibit the expression of specific genes. Recently, clinical studies using antisense RNA to treat lung cancer have been approved.

Pharmacology and Chemistry

NIGMS supports the bulk of NIH-funded basic research in chemistry, especially those studies aimed at total synthesis of natural products. One such product is the promising anticancer drug taxol, which is currently derived from yew trees. Because each yew tree yields only a small amount of taxol and because the trees are in limited supply, scientists are racing to find ways to synthesize this compound in the laboratory. Many of the techniques that they are using were developed by NIGMS grantees. Interestingly, much of the current attention to taxol was stimulated by basic research done by an NIGMS grantee in the late 1970's, which showed that this drug works by interfering with the normal breakdown of microtubules. These structures have an important role in cell division, cell movement, and the transport of substances within the cell. Once taxol's mechanism of action was found, its potential use as a cancer chemotherapeutic agent became clear, and the National Cancer Institute began sponsoring studies using taxol.

Studies in basic chemistry affect all areas of biomedical research. These studies aim to uncover the chemical patterns and rules that underlie the functioning of biological molecules.

Understanding these rules can lead to new synthetic substances that are able to carry out delicate chemical transformations. One goal of chemists is to learn how to "engineer" enzymes to provide greater control over chemical reactions, prevent the synthesis of unwanted byproducts, and produce drugs more quickly and less expensively than is now possible.



"As we develop a more complete understanding of cellular and molecular disorders, we can look to the emergence of a whole new basis for the practice of medicine." Dr. DeWitt Stetten, Jr. (NIGMS director 1970-1974)

An example of this work is the invention of molecules called "chemzymes" by a Nobel Prize-winning NIGMS grantee. The first chemzymes that have been produced are designed to help eliminate one of the most persistent roadblocks to efficient, cost-effective chemical synthesis: the creation of a product that is a mixture of molecules having two different spatial orientations. Molecules of only one of the orientations are needed to perform the desired task, and, while the opposite form may have no effect, often it can cause adverse reactions ranging from mild to severe. The ability of chemzymes to make every molecule of a product in the same biologically effective orientation could have an important impact on the pharmaceutical industry, as well as on basic research.

In addition to studies of basic chemical principles, NIGMS-supported scientists have learned much about how specific types of drugs act on the body. In the 1970's, in studies that had the long-range goal of limiting drug side effects, an NIGMS grantee discovered proteins involved in the cell's response to light, hormones, drugs, neurotransmitters, and other outside signals.

He named them "G" proteins after the DNA building block, guanine, to which they bind. Since this discovery, he and other scientists have found many more G proteins and have begun to explore the tantalizing clues linking these proteins to cancer, diabetes, high blood pressure, and other disorders.

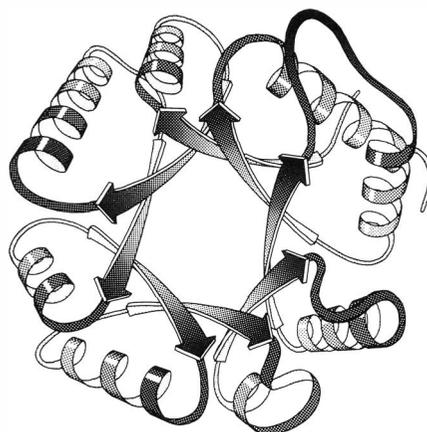
Research on immunosuppressants, drugs that are useful in preventing organ transplant rejection, is revealing new information about the activities of the immune system. This work not only promises to help researchers develop better immunosuppressant drugs, but also may

(Continued on Page 10)

(Continued from Page 9)

help them understand how immune cells are normally rallied to attack foreign substances. NIGMS grantees have discovered that both cyclosporin A, a drug that has revolutionized transplantation therapy, and a newer immunosuppressant, FK506, work by acting on specific immune system cells in a similar way, even though their physical structures differ. In their studies, the scientists found an enzyme to which both drugs bind. Further research on this enzyme should yield important information on the structural requirements for the action of immunosuppressants.

Since the introduction of anesthetics into medicine over a century ago, the mechanisms underlying the actions of these agents have been poorly understood. Recent technological advances, most notably the development of



Pyruvate Kinase domain 1

A schematic diagram of a protein structure obtained through x-ray crystallography (Courtesy of Dr. David Richardson and Jane Richardson).

Much of our current understanding of the detailed mechanisms by which large biological molecules function has come from the techniques of structural biology, such as x-ray crystallography and nuclear magnetic resonance spectroscopy.

Scientists seek to determine the structures of biologically important molecules like DNA, RNA, and proteins because, to a large extent, a molecule's structure determines how it functions. Since it is not possible to "read" amino acid sequences in such a way as to predict the detailed three-dimensional structure of large molecules, researchers use a variety of special techniques to arrive at this information. These techniques—including x-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy—have improved considerably in recent years, enabling scientists to decipher structures rapidly and more precisely. In addition, faster and less expensive computers are giving researchers new ability to handle enormous quantities of data and—through computer graphics—to visualize the structures and movements of proteins.

For example, a team of researchers led by an NIGMS grantee has provided the first three-dimensional structure of a protein kinase, one of an important class of enzymes that play roles in growth, neurotransmission, hormone signaling, and malignant transformation. As this work further elucidates the mechanism of action of protein kinase, it is anticipated that it will have rapid application in many areas, including a more detailed understanding of the development of such diseases as cancer and cholera.

NIGMS also supports research on the structure of the proteins of the human immunodeficiency virus (HIV) and the application of this information in targeted drug design. This program has had a number of achievements, including the determination of the detailed structure of an enzyme, reverse transcriptase, that is essential to the HIV life cycle; the

structure of the part of the receptor protein through which HIV infects the body; and a new method for the identification of compounds that might bind to, and thus inhibit, HIV. These accomplishments are expected to enhance the search for HIV-blocking compounds. A related NIGMS initiative supports the design of chemical strategies to synthesize promising HIV inhibitors more efficiently and cheaply.

Trauma, Burn Injury Research

NIGMS funds a program of research aimed at achieving a better understanding of the complex body responses that follow severe injury. The goal is to learn more about the basic molecular, biochemical, physiological, and endocrinological responses to various forms of trauma.

Basic scientists working in such fields as biochemistry, physiology, and immunology often collaborate in special trauma and burn research centers with medical specialists who provide patient care. They work together so research advances can be quickly applied to the treatment of patients. Years of scientific investigation in this area have led to remarkable improvements in burn and trauma treatment.

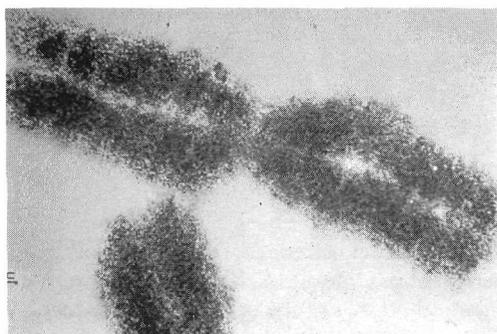
For instance, treatment has now been significantly improved for patients with massive, life-threatening infections caused by bacterial toxins. Research by NIGMS grantees has shown that if a patient suffering severe trauma is given an oral feeding (as opposed to an intravenous one) within hours of the injury, the incidence of these infections can be reduced substantially, permitting more rapid and complete recovery.

Tools for Research

In the course of their studies, NIGMS grantees often develop new research tools. Often, these tools are spin-offs from research that began as an attempt to understand some basic principle. For example, an NIGMS-supported scientist developed a new method for amplifying DNA for basic investigations and clinical diagnosis. The technique, called the ligase chain reaction, is particularly valuable for detecting small changes in DNA sequences, and holds great promise for increasing the accuracy of diagnostic tests for a number of diseases.

Other grantees are working on a powerful experimental tool, both for basic research and for clinical applications, called fluorescence *in situ* hybridization. This tool, which enables scientists to visualize multiple DNA sequences of interest at one time, could increase the speed and accuracy, and thus reduce the cost, of detecting particular genetic sequences, leading to the development of diagnostic tests for genetic diseases.

NIGMS-supported studies on basic genetic mechanisms led to the recent ability to create mice in which a specific gene has been inactivated. These so-called "knockout" mice are already being used in research on genetic disorders, most notably cystic fibrosis, where they represent the first animal model for this

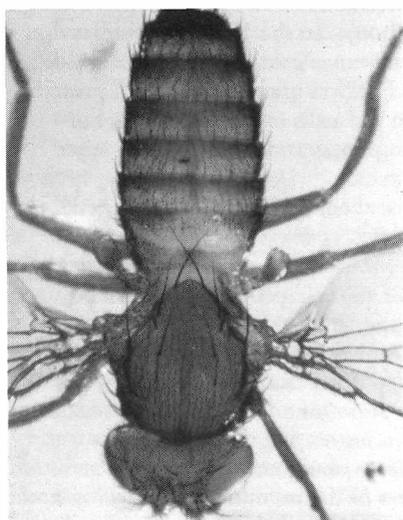


Micrograph of DNA condensed in a chromosome

artificial membranes, have provided new opportunities for scientists studying anesthetic action. NIGMS-supported researchers are now moving closer to identifying and characterizing specific receptors for anesthetics in the brain, which should lead to the design of safer anesthetics.

Biophysics and Molecular Structure

Another area in which NIGMS plays a pivotal role is the support of research that determines molecular structures at atomic resolution.



A mutant male fruit fly, Drosophila melanogaster, with extra body segments. Homeoboxes were first discovered in fruit flies.

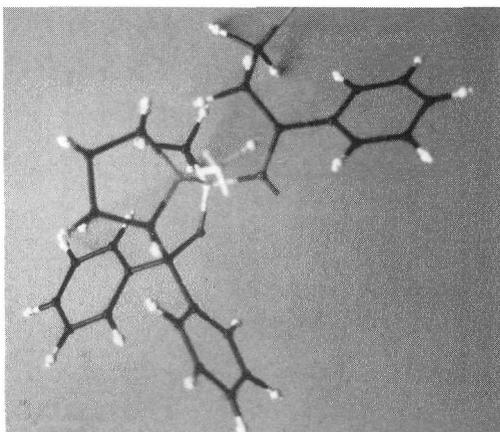
disease. The mice have also been used in studies on normal development, immunology, and learning and memory.

Resources for Research

Throughout the years, NIGMS has responded to the needs of the scientific community by providing critical resources for research. In 1972, the institute created the Human Genetic Mutant Cell Repository at the Coriell Institute for Medical Research in Camden, N.J. The repository establishes and stores cell lines from patients with well-characterized genetic disorders and from members of their families. These cell lines, along with detailed background information, are provided to requesting investigators at a modest charge. By using cells from the repository, scientists can study rare disorders in their own research settings without first having to locate a cell donor.

As genetic sequencing became increasingly common, NIGMS responded to the need for a means of storing newly discovered sequences in a data base from which they could be easily

retrieved. The institute founded GenBank, a computerized nucleic acid sequence data bank, in 1982. During the past decade, the number of sequences stored in GenBank has increased exponentially. On Oct. 1, GenBank became part of the National Library of Medicine's National Center for Biotechnology Information.



A model of a chemzyme taking part in a chemical reaction. This particular reaction can produce fluoxetine, a drug that may be useful in treating depression, chronic pain, and eating disorders.

retrieved. The institute founded GenBank, a computerized nucleic acid sequence data bank, in 1982. During the past decade, the number of sequences stored in GenBank has increased exponentially. On Oct. 1, GenBank became part of the National Library of Medicine's National Center for Biotechnology Information.

The Future

In reflecting on the institute's 30th anniversary, Kirschstein says, "NIGMS is proud to have contributed to the 'biological revolution' of the past few decades. We look forward now to being able to build on this beginning, to further develop our understanding of fundamental life processes so that we will be able to prevent, treat, and cure many of the diseases that still evade our control."

As physician-author Dr. Lewis Thomas wrote, in stressing the importance of basic biomedical research, "There is an abundance of interesting fact relating to all our major diseases, and more items of information are coming in steadily

NIMH Study Needs Healthy Kids

The Child Psychiatry Branch, NIMH, is recruiting healthy, normal-behavior boys and girls ages 5-12 to participate in a safe, noninvasive brain-imaging study using magnetic resonance imaging (MRI). Children may not wear orthodontic braces or have any learning disabilities. Total time commitment is approximately 6 hours over 2-3 visits. Benefits include free physical exam and MRI, pay, and an educational experience—kids will receive a souvenir picture of the brain. Call 496-3175 and leave message. □

Federal Employees Health Benefits Program Open Season, Nov. 9-Dec. 14

The Office of Personnel Management has announced an "open season" for Nov. 9 through Dec. 14, under the Federal Employees Health Benefits Program (FEHBP). During that period, eligible employees may change their plan, option, type of enrollment, or any combination of these. Note that the National Treasury Employees Union (NTEU) will drop out of the program after Dec. 31, 1992. Employees enrolled in NTEU will need to enroll in a new plan during open season or they will be without FEHBP coverage after Jan. 9, 1993. In considering their options, employees should be aware that they may not be covered as an employee under their own enrollment and as a family member under someone else's enrollment in FEHBP. Likewise, a member of one's family cannot be covered under more than one enrollment in the program.

Commissioned officers, employees serving under appointments limited to 1 year or less and intermittent employees are not eligible for enrollment in FEHBP. However, temporary employees who have completed 1 year of current continuous employment, excluding any break in service of 5 days or less, are eligible to enroll.

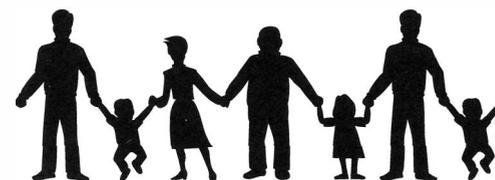
Employees eligible to participate in the open season will receive a booklet entitled 1993 Enrollment Information Guide and Plan Comparison Chart, from their personnel office. This booklet contains open season enrollment instructions, general information about FEHBP, the major features of all plans, and general categories of coverage such as dental and vision care, outpatient and inpatient service, calendar year deductible, hospice care, etc.

For 1993, plans have expanded the availability of preferred provider networks and increased the incentives to use them. In addition,

Tuberculosis Is Subject Of 'Science for All' on Nov. 19

The Staff Training in Extramural Programs (STEP) committee will present a "Science for All" lecture entitled "The Re-emergence of Tuberculosis," on Nov. 19, from 1:30 to 3:30 p.m. in Wilson Hall, Bldg. 1.

Dr. Barry Bloom, professor of microbiology and immunology at Albert Einstein College of Medicine in New York will discuss the clinical aspects of the disease. Epidemiologic and public health issues will be described by Dr. Alan R. Hinman, director, National Center for Prevention Services, CDC. Dr. Zeda F. Rosenberg, assistant to the director, NIAID, will present information about NIH's role in control of TB and how that role relates to other federal agencies. The "Science for All" series, designed for NIH staff without science backgrounds, is open to all NIH personnel. No advance registration is required. Sign language interpretation will be provided. For more information call 496-1493. □



tion, enrollees will see better benefits in the following areas: expanded preventive screening measures to include early detection of prostate and colon/rectal cancer; elimination of lifetime ceilings on prescription drugs; and more consistent out-of-pocket catastrophic limits for covered expenses for medical, surgical and mental health benefits. The requirement for precertification before a hospital admission, which was instituted in 1991, remains in effect.

Enrollees will be mailed a 1993 brochure by their current health benefits carrier. Employees who are eligible for enrollment and are not currently enrolled or covered by a federal plan should contact their personnel office for information on the program or plan brochures.

FAES Also Holds Open Season

The FAES Health Insurance Program will hold an open season Nov. 2-30. The program is open to: visiting fellows, full-time NIH employees who are not eligible for government plans, and full-time special volunteers and guest researchers. Open season is for those people who did not enroll when first eligible and for current subscribers to make changes. FAES is offering two programs this year—Blue Cross/Blue Shield Preferred Advantage, and M.D. IPA, a health maintenance organization. Information about rates and benefits, which will be effective Jan. 1, 1993, may be obtained from the FAES business office, Bldg. 10, Rm. B1C18. □

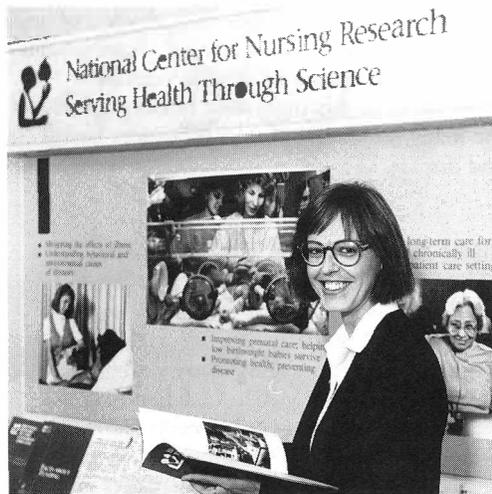
Scientist from Spain Learns Nursing Research Ropes

Like Christopher Columbus before her, Dr. Teresa Icart-Isern has come from Spain to the New World to make a discovery. In her case, she landed at the place she anticipated—the National Center for Nursing Research. She seeks to discover how NCNR operates, and how the NIH grant process functions. Her goal is to help set up a similar NCNR in Catalonia, Spain. Catalonia is in the northeast, near France, and forms part of the Mediterranean Coast.

Although her task will be challenging, fortunately this Spanish explorer is a true Renaissance woman when it comes to health and science. Icart's degrees include R.N., M.D., and M.S. in public health. As a full-time professor at the University of Barcelona, she teaches public health, specifically epidemiological methodology, to nursing students and nursing research to students seeking their master's degrees. As yet, Spain does not have a Ph.D. in nursing, although students frequently continue their studies in related specialty areas. In the United States, Ph.D.s in nursing have been awarded since the early 1930's, but schools of nursing with these doctoral programs were not widespread until the mid-to-late 1970's.

Icart's office is in the Division of Extramural Programs in the Westwood Bldg., where she is witnessing nursing proposals being evaluated and grants being awarded. She is also visiting directors of nursing research at universities to learn about curricula in graduate and post-graduate programs.

The importance of nursing first became apparent to Icart as she was growing up in Uruguay, known to Europeans as the Switzerland of South America. Nurses had university degrees in nursing and received considerable recognition for their role in primary health care. When she returned to Spain at age 20, she began her nursing education. Then she studied to become an M.D. while working as a nurse. Icart also received a scholarship to study in Brussels for her master's degree in public health.



Dr. Teresa Icart-Isern

Following additional courses at London's School of Hygiene and Tropical Medicine, she ultimately became a professor of nursing at the same time the profession was being integrated into Spain's university system.

Icart's "Ferdinand and Isabella," who made her journey to the new world possible, were Dr. Xavier Gonzales from the Health Studies Institute, part of the autonomous government of Catalonia, and Dr. Anna Roige, director of the department of nursing and public health at the University of Barcelona. Gonzales, an enthusiastic supporter of nursing research, spent a year at NIH, during which he visited NCNR. Following Gonzales's conversations with NCNR director Dr. Ada Sue Hinshaw, Icart received an invitation to visit the center. Thanks to some friendly persuasion by Roige, she was awarded a grant to make the trip by her government's Commission of Interdepartmental Research, Innovation & Technology, and the University of Barcelona agreed to continue to pay Icart's salary while she is away.

An advocate of yoga who enjoys painting, theater and the cinema, Icart lives on the NIH campus. □

Hunters and Hikers: Ready for Tick Season?

While it's hard to resist the allure of wooded areas and grassy fields, be aware that some uninvited guests may be sharing your picnic site. Tiny deer ticks can harbor the organism that causes Lyme disease. A new brochure is available that discusses what is known about this tick-borne disorder and offers tips to help minimize the danger of contracting it.

Lyme disease has been reported in virtually every state in the continental United States. The disease often produces a characteristic rash and painful, swollen joints. Many steps can be taken to prevent it. The disease is easily treated with antibiotics, particularly in the early

stages. Left untreated, however, it can progress to chronic arthritis and disorders of the central nervous system and heart. Preventing the disease and recognizing the signs and symptoms if it occurs are, therefore, of paramount importance.

Lyme Disease: The Facts, The Challenge is a joint publication of NIAID and NIAMS. The 20-page brochure is especially useful in identifying preventive measures, the array of symptoms, current diagnostic tests, and available treatments for various stages of the disease. For a free single copy, write to: Lyme Disease Booklet, NIAMS/NIH, Box AMS, 9000 Rockville Pike, Bethesda, MD 20892.

From Voice to TTY

Relay Service for Deaf Available

What happens when you need to call a deaf colleague in another building on campus or a deaf coworker at home, and you don't have access to a TTY? The answer? You don't. That was before the Maryland Relay Service (MDRS) was operational. This new telecommunication relay is provided 24 hours a day, 7 days a week, and allows anyone to place a call to or receive a call from any TTY user in the state.

When you make a voice call through MDRS, the relay customer agents will type on the TTY to relay your conversation with the deaf, hard-of-hearing or speech-impaired person. These agents are skilled in typing, grammar and spelling to meet the unique needs of relay customers. All calls are kept confidential.

In the past, deaf employees could only call individuals who had TTYs or had to rely on the goodwill of a coworker to place a voice call for them. Similar services are now offered in many other states.

Relay services are available by calling the numbers listed below:

- MDRS (Maryland)—1-800-735-2258 (TTY/Voice)
- Virginia Relay—1-800-828-1120 (TTY) 1-800-828-1140 (Voice)
- DC relay—202-855-1234 (TTY) 202-855-1000 (Voice) □

DCRT Computer Training Classes

| Classes | Dates |
|---|--------------|
| Networks for the Scientific Community | 11/2 |
| Using the Internet | 11/2, 11/3 |
| C Language Fundamentals | 11/2-11/6 |
| Macintosh Dial-Up and Network Connectivity | 11/4 |
| LAN Concepts | 11/4 |
| Network Services | 11/6 |
| SAS Fundamentals I for Programmers | 11/9, 11/10 |
| Fundamentals of Unix | 11/9, 11/10 |
| Creating and Using Simple WYLBUR Command Procedures | 11/12-11/13 |
| SAS Fundamentals II for Programmers | 11/12, 11/13 |
| SCRC Orientation | 11/16 |
| Kermit Scripts | 11/16 |
| GCG Sequence Analysis on the Convex | 11/16-11/18 |
| Welcome to the NIH Computer Utility | 11/17 |
| DB2: SQL and QMF Selected Topics | 11/17-11/19 |
| UNet, LAN, and Mainframe Mail Connectivity | 11/18 |
| Software Engineering and CASE Concepts | 11/19 |
| Thermodynamics Information in Laboratory Practice | 11/19, 11/20 |
| PC-DOS Advanced Topics | 11/23-11/24 |
| Andrew File System | 11/24 |
| Batch Files with PC-DOS | 11/25 |
| PC <—> Mainframe Communication with Kermit | 11/30 |

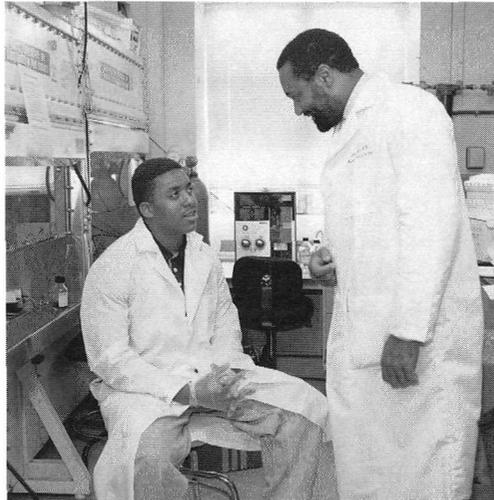
Classes are offered by the DCRT Training Program without charge. Call 496-2339 for more information. □

'Learn and Have Fun at Same Time,' Say Minority Summer Students

Learning about genes, neurons, enzymes, cell lines, DNA and RNA messengers; developing skills such as binding assays, pipetting, titrating, and micropipetting—these are just a few of many things that students who spent last summer at NIH participating in the Biomedical Science Career Orientation for Minority Students Program share in common.

"It was an opportunity to see another dimension of science," said Meredith Watson, who worked in the Laboratory of Biochemical Pharmacology, NIDDK.

"I was treated like a responsible scientist, while at the same time I was given the proper guidance and attention," said Antonio de Guzman, who worked in NINDS's Laboratory of Biophysics under the supervision of Dr. Vijay Kowtha.



Michael Sims works in NCI's gynecologic oncology section with his mentor, Dr. Eddie Reed (standing). "I am currently learning tissue culture techniques that I will use to study the cytotoxic effects of cisplatin on human ovarian cancer cells," Sims said.

"The program was designed to explore and evaluate the usefulness of work-oriented career awareness experience for selected high school students in influencing their career commitment. The feasibility and effectiveness of the program will be evaluated by participants as well as NIH staff with an eye toward making any adjustments that would improve METCON for next summer," said Diane Armstrong, OEO director.

Students were placed in a research laboratory under the guidance of a preceptor interested in promoting student career awareness and assisting young people in developing a strong and lasting interest in science, said Mutakabbir.

Students were encouraged to give oral and

written presentations; some of their reports were presented at a closing banquet held at Howard University.

METCON will conduct followup studies and evaluations to track the academic progress of the students in mathematics and science during their remaining high school years, their acceptance into college and their choices of a major upon entering college.

Arthurlina Clarke, who worked in NINDS's Laboratory of Molecular and Cellular Neurobiology, summed up the program this way: "I was both learning and having fun at the same time." □

Workshop Explores Environmental Health, Fairness of Risk Sharing

Pollution and environmental health risks—are they distributed equally across socioeconomic class and racial groups? If not, what are the health risks associated and what can government research agencies do to address these issues?

These questions were the focus of a recent workshop entitled "Equity in Environmental Health: Research Issues and Needs," jointly sponsored by NIEHS, EPA and the Agency for Toxic Substances and Disease Registry. Participants included scientists, policy makers, planners, and representatives from community groups from around the country.

Environmental equity is a multifaceted topic that includes issues such as race, socioeconomic class, occupation, differential exposure, and proximity of housing to environmental hazards such as major transportation corridors, pesticide use, and hazardous waste sites. The environmental issues discussed during the workshop were air pollution, water pollution, hazardous waste, and pesticides.

Also discussed were cross-cutting issues including biological susceptibility, data collection and evaluation issues, health status related to social class and/or minority status, and community perspectives on health and research needs. Each discussion will result in a peer-reviewed paper to be published in *Environmental Health Perspectives*, the journal of the NIEHS.

Planning is under way for a national symposium to be held in the Washington, D.C., area late in the summer of 1994. The national meeting will allow for a broad distribution of the research needs papers and will provide additional ideas and comments to be used by federal research and regulatory agencies.

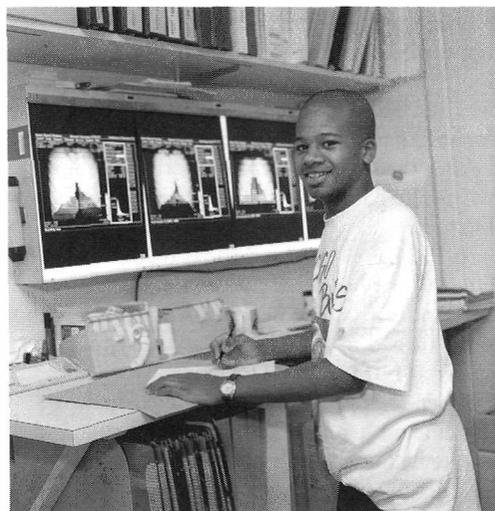
NIEHS will be the lead agency in planning the national meeting. A planning committee is now being assembled and input is welcome. Contact Jerry Phelps, NIEHS, (919) 541-4259. □



Guadalupe Quinteros worked in the CC's diagnostic radiology department under the guidance of Dr. Nilo Avila. "I have been exposed to the different modalities in the department, from mammography to magnetic resonance imaging and ultrasound," she said.

Kimberlee Goode viewed this as "an opportunity to participate in experiments and research that could change the world of science. It also instilled in me lessons in teamwork and flexibility." She also worked in NINDS's Laboratory of Biophysics.

These students were among a group of 21 who came to NIH under the auspices of the District of Columbia Metropolitan Consortium for Minorities in Engineering, Inc. (METCON), which coordinates scientific and engineering resources from local industries, federal agencies, community organizations and engineering schools. METCON, sponsored by Howard University, was overseen by NIH's Office of Equal Opportunity and supported by an award from the NIH associate director for minority programs, Dr. John Ruffin. Jalil Mutakabbir, Black Employment Program manager for OEO, served as NIH coordinator for the METCON students.



Jason Parris performs quantitative analysis of CAT scan images in Dr. Irwin Feuerstein's CAT reading area in the CC's diagnostic radiology department. "I am working on a research project to find normal lung density."

NINDS' John Hallenbeck Honored

The Undersea and Hyperbaric Medical Society (UHMS) recently honored Dr. John M. Hallenbeck, acting chief of the NINDS intramural Stroke Branch, with the UHMS's highest award.

The Albert Behnke, Jr. Award is given annually to an individual in recognition of outstanding scientific contributions to advances in the undersea and hyperbaric biomedical field. Hallenbeck recently received the award at the society's annual awards banquet in acknowledgement of his research spanning two decades.

His scientific endeavors have provided major advances in the understanding and treatment of decompression sickness and cerebral air embolism. In general, decompression sickness is a disorder characterized by joint pains, respiratory symptoms, skin lesions, and neurologic signs. It occurs primarily in aviators flying at high altitudes and in persons who have been breathing compressed air such as in underwater workstations and diving apparatus. Cerebral air embolism occurs during decompression when air bubbles enter systemic arteries and travel to the brain; it can also occur during trauma or surgical procedures in which air bubbles enter either arteries or veins. According to the UHMS, Hallenbeck's work "has enabled all who venture into the hyperbaric milieu to do so with greater safety and effectiveness."

The award from UHMS was given in recognition of Hallenbeck's research on the pathophysiological processes of decompression sickness and cerebral air embolism and his development of methods to treat them. In particular, Hallenbeck has characterized the role of platelets and leukocytes in producing abnormalities in the flow of blood in the central nervous system as a result of these diseases. He has also studied the effects of edema in the intracellular tissue spaces of the cerebrum caused by the same disorders.

"By dint of Dr. Hallenbeck's superb scientific undertakings, he has enhanced the safety and capability of divers, aviators, and the clinical hyperbaric medicine community," the UHMS said.

Hallenbeck earned his medical degree in 1966 from the University of Pennsylvania. He completed his neurology residency in 1970 at the University Hospital in Ann Arbor, Mich.

Before coming to NIH, Hallenbeck was chairman of neurology at the National Naval Medical Center in Bethesda.

Hallenbeck focused his research career in the Navy primarily on diving physiology and undersea medicine with a major emphasis on the cause and origin of spinal cord-damaging decompression sickness. During this time, Hallenbeck also developed a strong interest in cerebrovascular disease.

Another area of interest for Hallenbeck is



Dr. John M. Hallenbeck

studying damaged tissues resulting from arterial gas embolism. Arterial gas embolism is the sudden blocking of an artery by a gas bubble. The scientific and medical parallels of arterial gas embolism and stroke led Hallenbeck to use the gas embolism model as a means to investigate the pathophysiology of stroke.

In addition to his extensive research duties at

NIH, Hallenbeck also imparts his knowledge to future research scientists and other physicians by teaching at the National Naval Medical Center and serving on the faculty of the Uniformed Services University of the Health Sciences, where, for the past 9 years, he has been professor of neurology and physiology and where he has held the offices of vice chairman and chairman for research in the department of neurology (1983-1991).

Hallenbeck's many accomplishments and research activities have been publicly appreciated in the past. In 1975, he received the Stover-Link Award for Significant Contributions to Biomedical Research in Support of Undersea Activities, and in both 1977 and 1980 he received the Naval Medical Research Institute's Most Significant Publications Award.

Hallenbeck is currently a member of NINDS' internal review board and serves as a consultant to NASA. From 1986 to 1991, he was an ad hoc member of the National Advisory Neurological Disorders and Stroke Council.

His many memberships in professional societies include the Society for Neuroscience, the American Neurological Association, and the American Academy of Neurology.—Shannon Garnett □

DFM'S Frieda Egber Retires After 30 Years in Government

Frieda Egber is retiring after 30 years with the U.S. Navy and NIH. Her career here has been with the Operations Accounting Branch in the disbursing section and the classification and processing (C&P) unit.

Egber started her government career with the Navy in 1944 at the Philadelphia Navy Depot, where she was the youngest civilian employee ever hired. She had to obtain working papers to get hired and was known as the "Darling of the Navy." She would not divulge her age when she started working.

During her 8 years with the Navy, Egber was responsible for storing and providing spare parts for "Hellcat" aircraft used on aircraft carriers. It was her job to ensure that parts were available for shipment to the carriers in the Pacific Fleet.

After the war, she went to work in disbursing where she paid all of the bills for the 4th Naval District.

In 1954 she left government service to raise a family. She has three children, Mitchell, Carol and Andrew. Once her children were in school, she returned to government service and a new career at NIH.

When she applied for a job here, she wrote one line on her SF-171 that said, "I paid and audited all of the bills for the 4th Naval District." She was hired on the spot as a temporary employee. She was a temporary for 3 years until OPM told NIH to either hire her or let her go. She then became a full-time employee.

After 4 years in C&P, Egber transferred to the disbursing section, paying bills for NIH. For 4



Frieda Egber

years she worked in this post, rising to assistant supervisor in the days when everything was done manually.

She then returned to C&P where she remained until her retirement. During this period she was promoted to lead accounting technician, touching the lives of many with her knowledge, friendliness and willingness to help those in a bind. Many will miss this source of information and assistance that they have come to rely upon.

In retirement, Egber plans to spend time with her two grandchildren, Merrick and Alexander, and travel to such places as Atlantic City and Florida. □



TRAINING TIPS

The NIH Training Center, Division of Personnel Management, offers the following "hands-on" IBM and Macintosh computer courses:

| <i>Personal Computing Training Course Titles</i> | <i>496-6211 Starting Dates</i> |
|--|--------------------------------|
| Welcome to Macintosh | 11/9, 11/25, 12/11 |
| Advanced Macintosh Techniques | 11/18 |
| MacWrite | 11/30 |
| Intro to WordPerfect 2.0 (Mac) | 11/17 |
| Advanced WordPerfect 2.0 (Mac) | 12/2 |
| Intro to Microsoft Word 5.0 | 12/7 |
| Excel- 4.0 Level 1 | 11/16 |
| Lotus for Mac - Level 1 | 12/1 |
| Intro to Filemaker PRO | 12/3 |
| FoxBASE 2.01-Level 1 | (upon request) |
| FoxBASE 2.01-Level 2 | (upon request) |
| MacDraw PRO | 12/10 |
| 3Com PC Network-Level 1 | 11/16 |
| 3Com PC Network Management | (upon request) |
| Intro to Personal Computing for New Users | 11/20 |
| Disaster Recovery and Data Retrieval for the PC | 11/13 |
| Introduction to DOS 5.0 | 11/20, 12/7, 12/18 |
| Introduction to Windows 3.0 | 11/9, 11/23 |
| WordPerfect for Windows | 11/10, 11/17, 12/9 |
| Introduction to WordPerfect 5.1 | 11/3, 12/8 |
| WordPerfect 5.1 - Advanced Topics | 11/16, 12/14 |
| Advanced Paradox | 11/24 |
| Introduction to dBASE III+ | 11/4 |
| Lotus for Windows | 12/15 |
| IMPACT System for Personnel Staff | 11/3, 12/1 |
| IMPACT System for MSCs | 11/9, 12/4 |
| IMPACT System for Admin Staff | 11/23, 12/16 |
| IMPACT System for Professional Staff | 11/23, 12/16 |
| Introduction to CRISP | 10/30, 12/11 |
| Advanced CRISP | 12/11 |

NIEHS Targets Four Research Priorities

Four priority areas for environmental health sciences research were identified recently by Dr. Kenneth Olden, NIEHS director, who unveiled them at a recent meeting of the National Advisory Environmental Health Sciences Council.

Briefly, the areas are:

Basic mechanisms of environmental disorders, that is, the understanding of the molecular and genetic basis of environmentally caused disorders: Recent advances in molecular biological techniques will enable scientists to develop a more detailed understanding of the interaction of environmental agents at the level of basic cell function. The institute is particularly interested in looking at the role of molecular receptors in toxicity. Other areas of special interest include mechanisms related to programmed cell growth and death, genetic susceptibility and predisposition to disease, and events controlling differentiation and development of organs and tissues in embryos and fetuses.

Environmental causes of diseases of public health import: Identifying causative agents of environmental disease has proven difficult, and for disorders with suspected environmental components, increased research efforts are needed. Of particular interest are reproductive and developmental disorders, problems relating to aging, asthma and pulmonary fibrosis, neurodegenerative disorders (e.g., Alzheimer's and Parkinson's diseases), diseases involving the neuro-endocrine-immune axis, and cancer, particularly hormone-related cancers such as

cancers of the breast or prostate, and cancers related to exposure to DES.

Clinical studies and clinical research: The institute will increase its support for environmental health programs in clinical settings, particularly in evaluating strategies that could be used to prevent or intervene in environmentally associated diseases or disorders.

Enhanced science base for public policy decisions and health programs: Public policy makers are forced to make important decisions on environmental health issues, often with too little information. Better policy would result if the science base could be strengthened. Areas in which this base could be used include minority health and environmental equity questions; developing effective prevention and intervention strategies; biomarkers and risk assessment; and communications and technology transfer.

"These priority areas do not eliminate our other commitments," Olden explained, "but they provide a focus for advances in the most urgent and promising areas." He explained that each priority must meet three criteria—address an area ripe for exploration, where a positive outcome could be expected over the next 5 years; represent a real public health problem; and be an area in which NIEHS has a research strength.

For copies of *Human Health and the Environment: Some Research Needs* (Task Force 4); "Guidelines for Environmental Health Sciences Centers;" write: Office of Communications, NIEHS, Mail Drop B2-05, P.O. Box 12233, Research Triangle Park, N.C. 27709. □

Start Your Own LISTSERV Mailing List at NIH; DCRT Offers Help

Researchers who want to discuss specialized topics with others around the world are now able to start their own electronic exchange. Since 1986, people with access to the NIH mainframe computers or connections to NIHnet have been able to subscribe to LISTSERV computer mailing lists and participate in local and international dialogues. Now, those same individuals can create their own lists, thus establishing electronic mail discussion groups on topics of their choice.

LISTSERV is actually a mailing list manager that enables people with common interests to join electronic mail groups and discuss a variety of topics with other subscribers. Some lists have restrictions on who can join, while others are open to anyone. The most popular lists have hundreds of subscribers and may distribute dozens of mail items every day. Subscriptions are free.

Typically, members of LISTSERV send mail to "the list" and the software automatically distributes it to all the subscribers, though some list owners choose to edit the submissions. Similarly, subscribers receive a copy of mail that other members send to lists they have joined.

What information is available through LISTSERV? It provides access to thousands of lists that disseminate information on a variety of topics. A short sample of scientific lists includes:

- AIDS: scientific/medical AIDS news
- ALCOHOL: alcohol and drug studies
- BLIND-L: computer use by and for the blind
- DIABETES: an international research project on diabetes
- IMAGE-L: image processing and applications
- INFO-MAC: Macintosh digest
- NRSING-L: Nursing information
- SOREHAND: discussions of Carpal Tunnel Syndrome and Tendonitis

Access Technical Detail

Anyone on a local area network connecting to NIHnet can obtain a complete listing of LISTSERV lists, including short descriptions, by sending electronic mail to the address SERVER:WYLBUR; the subject line should read get dsn &public.listserv.lists. Others can order a copy of the list by anonymous FTP at

cu.nih.gov. Once users are connected, they must change to the LISTSERV directory to get the dataset LISTS. WYLBUR users can receive this list by accessing the WYLBUR data set &PUBLIC.LISTSERV.LISTS.

To join a list, find the address from the &PUBLIC.LISTSERV.LISTS data set and send electronic mail or an interactive message directly to LISTSERV.

Two manuals available from the DCRT Technical Information Office explain LISTSERV in more detail. Both *General User's Guide to the NIH LISTSERV Facility* and *List Owner's Guide to the NIH LISTSERV Facility* can be ordered through WYLBUR's ENTER PUBWARE, by calling 496-5431, or by stopping by Rm. 1015, Bldg. 12A.

To get more information about joining a LISTSERV list or about starting one, call the Training Unit, 496-2339, to schedule a consultation or register for the seminar, "LISTSERV Electronic Mailing Lists," on Dec. 1. □

Contract Launches Women's Health Initiative

The Fred Hutchinson Cancer Research Center in Seattle has been awarded a \$140 million, 15-year contract to become the clinical coordinating center of NIH's "Women's Health Initiative," the largest coordinated study of women's health undertaken. As coordinating center, the facility will oversee the work of what will ultimately be a network of 45 clinical centers nationwide carrying out the initiative.

For the last year and a half, the initiative has been in the planning and contract competition stages. The study will evaluate the effectiveness of various promising interventions in preventing a number of major diseases in older women. The full 15-year project, costing some \$625 million, is expected to involve more than 150,000 women.

The initiative will examine treatment and prevention strategies for coronary heart disease, cancer and osteoporosis, and includes both clinical and observational studies.

"The coordinating center will function as the central nervous system of the Women's Health Initiative," said NIH director Dr. Bernadine Healy. "The Seattle project will make certain that each clinical center holds to the highest scientific and administrative standards.

"The Hutchinson Center has extensive experience in coordinating large medical research trials, especially dietary interventions," she continued. "And it has distinguished itself in the management of other NIH clinical trials of women."

The first 15 of the 45 clinical centers will be named early in 1993, while the remaining 30 will probably be named early in 1994. The first 15 centers will develop, implement and refine the overall program for the initiative, which Healy called "the most extensive studies of women's health ever conducted."

The objectives of the clinical trials are to test the benefit and risk of hormone replacement therapy, dietary modification, and supplementation with calcium plus vitamin D on the overall health of postmenopausal women ages 50-79. With some overlap of participants in the different studies, approximately 57,000 women will participate in the clinical trials.

"The coordinating center will function as the central nervous system of the Women's Health Initiative."

The goals of the observational study will be to improve risk prediction of coronary heart disease, breast cancer, fractures and total mortality in postmenopausal women, to examine the impact of changes in characteristics on disease and total mortality; and to create a resource of data and biological samples that can be used to identify new risk factors and/or biomarkers for disease. Some 100,000 women will participate in this phase of the study. □

Annual Health's Angels Runs Set

On Sunday, Nov. 8 at 9 a.m., the NIH Health's Angels Running Club will hold its 17th anniversary run at the Ken-Gar Recreation Center in Rock Creek Park in Kensington. The run will include a 1-mile fun run for children 12 and under, a 2-mile fun run-for-your-life, and a 10-mile run. The 1-miler starts at 9 sharp, the 10-miler at 9:15 and the 2-miler at 9:20 a.m.

Ribbons will be awarded to runners in all events. Age group prizes plus special "unbody" awards and top NIH runners prizes will be awarded. Only runners with a ratio of weight (pounds) to height (inches) of greater than or equal to 2.5 will be eligible for "unbody" awards.

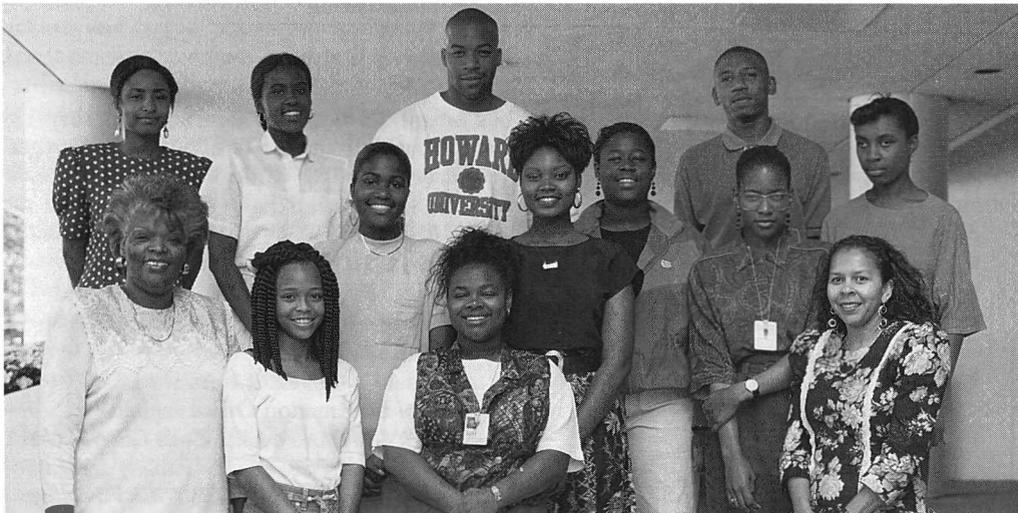
To get to Ken-Gar from NIH, go north on Rockville Pike for about 2 miles, turn right on Strathmore Ave. and follow it for about 2 miles. Turn left on Beach Drive and follow it under the railroad trestle. The Ken-Gar Rec Center will be on your right; park anywhere.

For more information or to volunteer to help staff the event, call Bob Brunner, 496-1038, or Jerry Moore, 496-4606. □

Tech 2000 Tour Scheduled

A guided tour of Tech 2000, a gallery of interactive multimedia, is planned for Nov. 5 by the NIH public affairs forum committee. The exposition, located at Techworld Plaza in downtown Washington, contains more than 60 hands-on applications of multimedia computer hardware, which the *New York Times* described as "the computer-age equivalent of a carnival midway." Visitors can put themselves through the Air Force's course for teaching ground crews how to put out a fire in an F-15 fighter, for one example, or for another, learn how to follow the motifs, movement by movement, in Beethoven's Ninth Symphony.

Space is limited for the tour. Cost is \$5 each. Call Joanne Belk, 496-5633, before Oct. 30 to reserve a place.



The first "class" of interns from the NIAID/Dunbar High School Partnership "graduated" this summer after working in laboratories in NIAID's Division of Intramural Research and in extramural offices. As they enter colleges and universities throughout the nation, NIAID will track their progress as they pursue careers in science, engineering, computer science and business. During the past year, NIAID has offered students of Dunbar High in Washington, D.C., lectures, tours of NIH, tutorial matching, library resources and faculty enrichment. In the future, these students will be eligible for NIAID's Introduction to Biomedical Research, a program designed to acquaint academically talented college minority students with career opportunities in this broad field. Pictured are (front, from l): Gwendolyn B. Brooks, NIAID EEO manager; Lakisha Hayes; LaShawn Allen; and Yvonne Hefley, NIAID EEO specialist; second row (from l): Tonita Harrington; Octavia Anderson; Theresa Crosland; and Tanisha Birth; and top row (from l): Ladrian Ingram, EEO office secretary; Shannon Joyner; James Witherspoon; Wyle Kynard; and Julia Smith.

Holiday Bazaar Scheduled, Dec. 8

Join the festivities on Tuesday, Dec. 8 from 11 a.m. to 4 p.m. when R&W presents the second annual Holiday Bazaar to benefit the Friends of the Clinical Center. The event will take place in the Visitor Information Center, Bldg. 10, and include gift items from holiday crafts to purses, jewelry, paintings, children's books, fresh wreaths, pottery, t-shirts, and more. Take care of holiday shopping and help Clinical Center patients, too. Don't miss this fun event. □