NINDS Scientists Speed Gene and Brain Research

By Frances Taylor

Using a novel strategy, scientists at the National Institute of Neurological Disorders and Stroke have isolated key identifying regions of more than 400 genes that work inside the human brain. The scientists say their work, reported in the June 21 issue of *Science*, should help identify genetic defects that cause brain disease and speed progress of genetics research.

Of all the DNA found coiled inside the nuclei of human cells, only about 3 percent consists of genes, or strips of DNA that hold blueprints for the proteins required for life. Some of these genes are active in all tissues while others are expressed only in certain parts of the body such as the heart, liver or brain. The number of genes expressed in the brain may be as many as 30,000 of the body's approximately 50,000-100,000 genes.

Sequencing studies examining the human genome generally sequence all of the DNA found inside each human cell. In the NINDS study, scientists sequenced only partial DNA from genes expressed in the brain, saying their strategy is a valuable advance in gene sequencing.

"If your aim is to sequence the genes, this [See BRAIN, Page 4]

EGAD—A Bright Idea

Collaboration Leads to Electronic Grant Revolution

By Gregory Wilson

Nearly 4 years ago, computer specialist Richard Feldmann was sitting in his office at the Division of Computer Research and Technology when John Mathis of the Division of Research Grants walked in with a problem: DRG was receiving 35,000 grant applications each year, all on paper, that were then photocopied 75 times and distributed to various offices. The paper load was becoming unmanageable. Wasn't it time, Mathis thought, to explore new processing strategies? Couldn't incoming applications be automatically routed to the appropriate study sections for evaluation?

The collaboration that followed is the story of EGAD, or electronic grant application development, an idea whose time has come.

Reducing the paper load would not be an easy task. There are 96 study sections committees of research scientists that evaluate the scientific merit of each application. Each committee has a different area of expertise, and handsorting tens of thousands of paper applications and trying to decide which com-

(See EGAD, Page 8)
Clown Polka Dots amused NIH'ers who lent their umal urong support to the ninth annual Camp Fantastic summer camp for children with cancer. Some 900 employees were ed. Held tmder threatening skies, this year's luncheon nonetheless netted more than $4,000 for the "Flash Fax," can score up to 1,000 documents is piloting a new technology available from in conjunction with the NIH Telecommunications Branch, Division of Technical Services, AT&T Bell Labs called the NIH Automated Network Connections.

This technology, announced in the January/February 1991 NIH Telecommunications Branch Network Connections and formerly called "Flash Fax," can store up to 1,000 documents in a small unit that sits near a telephone system control unit. When a caller accesses NIH ADDS, a touch-tone dial pad can be used to request a document to be sent to any fax machine within the NIH community. In approximately 5 minutes, the requested document, with a cover sheet, will arrive at the fax machine designated by the caller. NIH ADDS has obvious applications for paper-intensive organizations.

DMP is testing NIH ADDS using the NIH Manual Chapter Index and the NIH 16 Memo Index. Both documents are now available from DMP, which is testing NIH ADDS through August 1991.

DMP's anticipated use of NIH ADDS is expected to give the NIH community yet another option for obtaining current index information relating to NIH manual chapters and I&I memos. DMP plans to continue its involvement with the MANUALS bulletin board, using DCRT's Enter BBS since each system offers unique advantages to the user community.

For a copy of the instructions, call DMP, 496-4606, or read Bulletin 26 in the MANUALS bulletin board.

Bhorjee Joins DRG as SRA

Dr. Jaswant Singh Bhorjee, associate professor of cell and molecular biology, Meharry Medical College, has been appointed scientific review administrator of the pathology A study section in DRG's Referral and Review Branch. The section is one of 82 within the division. It consists of 20 members from the scientific community who conduct the initial scientific merit review of applications relating to studies in pathology, pathobiology, and the biochemistry of disease.

At Meharry, Bhorjee's research projects were supported by NCR and NIGMS; the National Science Foundation; and the Agency for International Development. He was also the recipient of an NHLBI faculty development award for studies of high mobility group proteins, growth factors, and myogenesis. Besides serving on several Meharry advisory and management committees, he has been a member of a grants review panel of the American Heart Association.

Before joining Meharry in 1984, Bhorjee was assistant professor of cell and molecular biology at the University of Illinois at Chicago. His research there was funded by a grant from NIH. During 1982-83, he served as an ad hoc member of the biomedical sciences study section, DRG.

The NIH Record

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Study Finds Systolic Hypertension Can Be Treated

By Carolyn Shanoff

Drug treatment can help prevent strokes in older people with isolated systolic hypertension (ISH), according to a study supported by the National Heart, Lung, and Blood Institute and the National Institute on Aging.

The results of the study, the Systolic Hypertension in the Elderly Program (SHEP), indicate that using a low dose of an inexpensive diuretic can cut the incidence of stroke by 36 percent and coronary heart disease by 27 percent among people with the condition. The findings have significant impact for older people because the prevalence of elevated systolic blood pressure increases with age.

Isolated systolic hypertension means that the systolic pressure, the pumping pressure of the heart as it pushes blood into the arteries, is elevated, while the diastolic blood pressure, the resting pressure of the heart between beats, is normal. A systolic reading over 140 is considered high.

At a news conference in Wilson Hall, Dr. Claude Lenfant, NHLBI director, said that the dramatic reductions in strokes, coronary heart disease and left ventricular failure among study participants were achieved with very few adverse side effects using the lowest effective doses of antihypertensive drugs.

According to Dr. Jeffrey Probstfield, coordinator of the study for NHLBI, treatment for ISH with the diuretic chlorthalidone is simple and inexpensive. When it alone is not sufficient to control the condition, he said, a beta adrenergic blocking drug such as atenolol may be added as long as there are no indications to the contrary.

This treatment of isolated systolic hypertension can result in 24,000 fewer strokes and 50,000 fewer incidents of severe cardiovascular problems, including heart attacks, each year, Dr. T. Franklin Williams, NIA director, told reporters at the press briefing. "Clinicians must offer this treatment to older patients as quickly as possible, not only for its benefits to the individual, but also for its positive impact on our approach to health care and on cost containment," he said.

Nearly 4 million Americans over age 60 have elevated systolic blood pressure. That includes 7 percent of people ages 60 to 69, 13 percent of those 70 to 79, and 20 percent of those 80 to 89. The number of older people with this condition is expected to top 8 million by the year 2025.

In the past, Williams said, physicians were reluctant to treat ISH in older people because they thought it was a natural consequence of aging. The SHEP study is the first clinical trial to demonstrate the possible health benefits of lowering isolated systolic hypertension in older people.

SHEP, a randomized, double-blind, placebo-controlled study, was conducted at 16 clinical centers across the country. Nearly 5,000 men and women participated in the 5-year study beginning in 1984.

IL-2 Toxin Effective Against HIV-Infected Cells

A genetically engineered bacterial toxin has been used to kill cells infected with the AIDS virus while leaving healthy cells unharmed, reports a team of researchers. The "targeted toxin" could eventually have therapeutic potential for individuals infected with the AIDS virus, say the investigators.

The team, led by Drs. Robert Finberg of the Dana-Farber Cancer Institute in Boston, Sharon Wahl of NIDR and Jean Nichols of Seragen Inc. in Hopkinton, Mass., reported their findings in the June 21 issue of Science.

The human immunodeficiency virus (HIV), which causes AIDS, attacks certain cells critical to proper functioning of the immune system. Infection by HIV activates the cells, triggering them to produce a molecule on their surface called the IL-2 receptor. The receptor is not found on unactivated cells. By taking advantage of this molecular difference between HIV-infected and uninfected cells, the investigators selectively destroyed HIV-infected cells in culture while sparing cells that did not have the receptor.

They exposed the cells to a toxin that specifically targets the IL-2 receptor. The toxin is a genetically altered diphtheria toxin. In its natural form, diphtheria toxin attacks a wide range of human cells.

The toxin used in these studies has been genetically altered so that it attacks only cells bearing the IL-2 receptor. Like natural diphtheria toxin, the altered toxin works by entering the cell and interrupting protein synthesis, ultimately leading to cell death.

The scientists tested the targeted toxin on mixed cultures of HIV-infected and uninfected immune cells. They examined two types of cells: T cells, which are the primary target of HIV, and monocytes, which serve as reservoirs of infection and allow the virus to spread throughout the body.

"We are able to show that this toxin selectively kills HIV-infected T cells and monocytes and inhibits production of viral proteins and infectious virus," said NIDR's Wahl.

The use of specifically targeted toxins is a logical method for eliminating HIV-infected cells without harming the patient, she noted. The IL-2 toxin has been used by Seragen in other studies for the experimental treatment of certain cancers in which the tumor cells bear the same IL-2 receptor found on HIV-infected immune cells. The results have been promising in reducing tumor size.

Based on the results of their laboratory studies and the cancer treatment evidence, the investigators believe the IL-2 toxin may have potential as a treatment for individuals infected with HIV. While they caution that the toxin would not be a cure for AIDS, it could decrease the number of infected cells, thereby reducing viral replication and the total amount of virus in the body.

The researchers caution that additional studies are needed to determine whether the IL-2 toxin can be safely administered to HIV-infected individuals.

Also collaborating on the study with Finberg, Wahl and Nichols was Dr. Janice Allen of NIDR. —Wayne Little
strategy is fast, efficient and cheap,” said Dr. J. Craig Venter, chief of NINDS’s receptor biochemistry and molecular biology section. “Using our strategy, we can obtain a unique DNA region that identifies the gene over a very short time and at a cost of about $48—a fraction of what sequencing 100 percent of the DNA will eventually cost.”

These unique regions, called expressed sequence tags (ESTs), are stretches of sequenced DNA taken from separate genes. Venter said they offer scientists a shortcut in their genetic research. Much in the same way that police use fingerprints to identify suspects for a crime, scientists can use the tags to identify a gene quickly and efficiently.

“Normally if you sequence DNA from cells, it’s very difficult to tell where the genes are,” said Venter. “But if you have tags and know their nucleic acid sequence, you can spot the genes hidden in a long strand of sequence. You can also tell if the gene is expressed in the brain.”

Of the 466 tags that were located and sequenced in the study, more than 330 represent new human genes. NINDS scientists found that 48 of these new genes closely matched known genes from other well-studied species, including yeast and fruit flies. They now plan to collaborate with other scientists in uncovering the role of the additional new genes.

Sequenced ESTs could also speed mapping of disease genes that affect the brain such as the gene for Huntington’s disease, Venter said. “It will help those looking for the cause of genetic disorders,” he predicted, “because we can immediately map the ESTs onto the chromosomes.”

For example, Venter explained, if one of the ESTs were to map to the chromosomal region suspected of containing the Huntington’s disease gene, then the sequenced brain gene would immediately become a possible candidate for causing the disease. Thus far, NINDS scientists have mapped 46 ESTs to human chromosomes.

Of the estimated 4,000 genetic diseases, one in four affects the brain and nervous system. Besides Huntington’s disease, neurogenetic disorders include such diseases as neurofibromatoses, muscular dystrophy and Alzheimer’s disease.

“The identification of ESTs could make a significant contribution to the analysis of human genes,” said Dr. Elke Jordan, deputy director of the National Center for Human Genome Research. “Dr. Venter is one of the first to demonstrate the usefulness of automated commercial sequencers in obtaining large amounts of DNA sequence information.”

“ESTs will boost efforts to sequence the human genome,” Venter said, “and work on sequencing key regions of all the genes expressed in the brain should continue to sequence all of the DNA, since areas that are not expressed genes will also contain important information about health and disease.”

Venter said he and his colleague Dr. Mark Adams will now sequence ESTs for the rest of the expressed brain genes during the next 5 years—at a rate of 48 genes each day. “Nobody would have even considered embarking on something this ambitious before—this is the first time sequencing has been done on this scale. It represents a major advance in the rate we gain new information on the brain,” Venter said.

In Venter’s laboratory at NINDS, DNA sequencing is completely automated: a computer-controlled robot performs the “exacting and tedious” chemical reactions to produce the DNA; a computer scans and color codes the DNA base pairs; and the sequences are put back in order using several additional computers. “It requires a lot of equipment that you don’t find in most laboratories,” Venter said.

In the study, NINDS scientists working with colleagues at the National Institute of Mental Health took advantage of special collections—called cDNA libraries—to narrow their sequencing to expressed genes. These libraries contain genetic material derived from brain tissue by a complex process.

Whenever a gene is read to form a protein, the cell creates a temporary copy, called messenger RNA, with a nucleic acid sequence that nearly mirrors the original DNA. Starting with brain tissue, scientists extract this RNA, then use it to recreate the sequence of the DNA found on the original gene. The recreated DNA is called complementary DNA (cDNA), with each piece of cDNA corresponding to one gene and known as a cDNA clone. By using libraries of many such cDNA clones, NINDS scientists were able to bypass long stretches of DNA that are not used to make messenger RNA and, therefore, are not expressed.

NINDS scientists took more than 600 cDNA clones at random from three libraries, obtained partial sequences with automated techniques and isolated 466 ESTs. The remaining partial sequences were not sufficiently unique to be used as ESTs.

Kramer Appointed Associate Director Of NCI Community Program

Dr. Barnett S. Kramer, who joined the National Cancer Institute in 1975 as a clinical associate, has been appointed associate director of the Early Detection and Community Oncology Program in the Division of Cancer Prevention and Control.

In 1978 after his 3-year fellowship in the Clinical Oncology Program, Kramer accepted a faculty appointment at the University of Florida College of Medicine. He returned to Bethesda in 1986 to become a senior investigator with the Navy Medical Oncology Branch and an associate professor at the Uniformed Services University of the Health Sciences; last year he was promoted to full professor. In addition to these two clinical and academic positions, for the last 2 years Kramer directed the institute’s medical oncology training programs.

Kramer will continue as clinical professor of medicine at USUHS, as well as a board member of the Physicians’ Data Query, associate editor of the Journal of the National Cancer Institute, and a member of several professional societies and organizations. As the new associate director, however, he will oversee the early detection studies, the community oncology and rehabilitation programs, the cancer prevention fellowship, and an intramural program in biomarkers and prevention research. His major scientific interests are cancer screening and early detection, intermediate endpoints in cancer progression, clinical trial methodology, and public health.
NIA Director Williams Announces Resignation

Dr. T. Franklin Williams, director of the National Institute on Aging since 1983, has resigned his position to return to appointments at the University of Rochester School of Medicine and Dentistry and the Monroe Community Hospital.

He said his return to academic life as professor of medicine and of community and preventive medicine will give him a chance to "help accelerate the integration of new knowledge about aging into the medical school curriculum and into the practice of medicine."

"It has been exciting to work with the NIA staff to enrich our understanding of aging processes and the common problems of older people," he said. "I will always take great pride in having participated in the growth of this institute and the continuing development of the field of aging research."

Williams said he is optimistic about the future of aging research. "Halting the Alzheimer's epidemic by learning what causes it and how to stop it before it starts should continue to be one of our highest priorities," he said in a recent interview. "Nerve growth factors in particular may have the potential for reversing damage to or spurring growth of nerves in the brains of Alzheimer's or Parkinson's patients. In fact, I'm particularly optimistic about a whole slew of growth factors, including those for connective tissue and bones, where we may be able to halt or reverse osteoporosis."

At NIA, he has encouraged physical fitness activities for the staff and is regularly in the Fitness Center in Bldg. 31 himself—early in the morning. He has also been a volunteer physician at the Washington Free Clinic and has helped recruit other physicians at NIH for the clinic.

Before coming to NIA, Williams had served for 15 years as a professor of medicine and of preventive and rehabilitative medicine at the University of Rochester. He also was codirector of the university's Center on Aging. His research and more than 90 publications have been concerned with metabolic diseases including hereditary rickets and diabetes mellitus, and a variety of aspects of the care of chronically ill and aging people.

He was elected to the Institute of Medicine of the National Academy of Sciences in 1976 and served for 3 years as a member of the institute council. He is a fellow of the American College of Physicians, the American Association for the Advancement of Science, the Gerontological Society of America, and the American Public Health Association, and a member of the Association of American Physicians and the American Geriatrics Society.

Among his recent honors are the doctor of science degree from the Medical College of Ohio, the Distinguished Service Award of the University of North Carolina, the Edward W. Gamble Award for Distinguished Service at the University of Rochester, the Distinguished Service Medal of the U.S. Public Health Service, the Distinguished Service Award of the Uniformed Services University of the Health Sciences, the Freeman and Kent Awards of the Gerontological Society of America, and the Henderson Award of the American Geriatrics Society, and the Freeman and Kent Awards of the Gerontological Society of America. He also has received the Distinguished Service Medal of the U.S. Public Health Service.

A native of North Carolina, Williams received his B.S. degree from the University of North Carolina, Chapel Hill, his M.A. from Columbia University, and his M.D. degree from Harvard Medical School. He received residency training on the Osler Medical Service of the Johns Hopkins Hospital and at the Boston Veterans Administration Hospital and was for 14 years a research fellow and member of the faculty at UNC-Chapel Hill.

Vaitukaitis Named NCRR Deputy

Dr. Judith L. Vaitukaitis has been appointed deputy director for extramural research resources, NCRR. She has served as director of the General Clinical Research Centers Program, NCRR, since 1986 and as acting deputy director for extramural research resources since February 1990.

"Dr. Vaitukaitis's accomplishments in NCRR program management assure us that she will be especially effective as we strive to direct research resources where they will be most productive," said NCRR director Dr. Robert A. Whitney, Jr.

She first came to NIH in 1970 as a researcher in the Endocrinology Branch, NCI. After additional postdoctoral training as a special PHS research fellow and as a senior staff fellow in the Reproductive Research Branch, NICHD, she was senior investigator and med-

Vaitukaitis received her M.D. from Boston University School of Medicine in 1966 and completed her internship and residency training at Cornell Medical Services, Bellevue Memorial Hospital, New York.

Dr. Judith Vaitukaitis

Kimberly B. Hooten recently was appointed chief administrative officer for DGERT. Before assuming her new position, she was the senior budget analyst at NIDDK, where she served the intramural division. Currently, she is an intern for the DHHS Women's Management Training Initiative, a highly selective year-long program. She also has worked for NCI and the U.S. Department of Agriculture.

Twins Needed for Study

A study at the Uniformed Services University of the Health Sciences needs twins age 8 and older; participants will be paid. Call (301) 295-3279.
NIA Grantee Wins Media Award

A training video aimed at hospital social workers who deal with Alzheimer's patients and their families has won a National Media Owl Award from the Retirement Research Foundation. The award was presented in Chicago recently at a dinner hosted by syndicated columnist Ann Landers and film critic Gene Siskel. The video was funded by a grant from the National Institute on Aging.

Produced at the Joseph and Kathleen Bryan Alzheimer's Disease Research Center (ADRC) of Duke University, the video, "Assisting Families of Patients with Alzheimer's Disease: Opportunities for Social Workers in a Hospital Setting," was cited for its careful portrayal of the problems facing caregivers of Alzheimer's patients when those patients are hospitalized for a separate medical condition. The Bryan ADRC is one of 20 ADRCs nationwide funded by NIA.

"The common goal of the ADRCs is to enhance research on Alzheimer's disease (AD) by providing a network for sharing new ideas as well as research results," said Dr. Teresa Stoss Radebaugh of NIA's Neuroscience and Neuropsychology of Aging Program. "This video will go a long way toward improving the care and assistance that Alzheimer's patients and their families receive from hospital staff when the patients are admitted for a different medical condition. We congratulate the Duke team for their outstanding effort."

According to Lisa Gwyther, education director of the Bryan ADRC, people with Alzheimer's disease require special treatment when they are hospitalized for other medical conditions. Hospital staff generally provide traditional medical care, she said, but not dementia-specific help with the demands of daily caregiving.

"Our experience," she said, "is that social workers generally are not prepared by education or experience to handle the unique problems posed by AD patients and their families in some health care settings. This video shows hospital-based social workers how to help families by identifying issues and potential strategies for daily care of the AD patient." Among the subjects the video tackles are emotional reactions of patients and their caregivers to hospitalization and how family caregivers can locate help and information once the patient returns home.

"We appreciate NIA's interest in funding the ADRCs to produce innovative training videos for direct care providers," Gwyther said. "These training aids can sensitize and inform social workers, and provide specific strategies to promote effective family care and coping."

That is important, said Gwyther, because the increase in the older population is likely to produce an increase in the number of

Film critic Gene Siskel (l) and syndicated columnist Ann Landers (r) flank Duke University's Elisabeth Hinman-Smith and Claiborne Clark, producers of a National Media Owl Award-winning training video for hospital social workers who deal with Alzheimer's patients and their families. The video was funded by the National Institute on Aging, which claimed its first Owl Award.

USUHS Study Needs Males

The Uniformed Services University of the Health Sciences needs healthy males for a study of effects of task performance on physiological functioning. Volunteers must be nonsmokers, nondrug users and between the ages of 18 and 45 for one 3-hour session. Compensation will be provided. For more information call (301) 295-3278.

New NIEHS director Dr. Kenneth Olden (r) greets HHS secretary Dr. Louis Sullivan and NIH director Dr. Bernadine Healy after his recent swearing-in ceremony. The event took place at NIEHS headquarters in Research Triangle Park, N.C.
Donald McRee Named NIEHS Branch Chief

Dr. Donald I. McRee has been named chief of the Scientific Review Branch in NIEHS’s Division of Extramural Research and Training. McRee’s branch is responsible for reviewing scientific and technical merit all research and development contract proposals and grant applications including those for program projects, research centers, special research grants, training grants, and applications received in response to requests for applications.

McRee joined NIEHS in 1969, 3 years after the institute was established as a division within NIH, and the same year NIEHS gained institute status. He came from Corning Glassworks Electronics Research Laboratory, in Research Triangle Park, N.C., where he was a senior research engineer, and had also served previously with the National Aeronautics and Space Administration in Langley Field, Va., as a research engineer. Prior to his appointment as branch chief, McRee was a health scientist administrator.

As a researcher at NIEHS for many years, McRee focused on the health effects of non-ionizing radiation, and took a leading role in NIEHS participation in United States-Soviet Union international agreements in the area of the health effects of microwaves, traveling 12 times to the Soviet Union and coordinating Soviet visits to the NIEHS facility.

McRee is on the graduate faculty and an adjunct professor in the School of Life Sciences at North Carolina State University in Raleigh. He is author and coauthor of more than 100 published scientific articles and abstracts and is the recipient of the NIH Director’s Award, the Public Health Service Outstanding Performance Award, and the Public Health Service Award in Recognition and Appreciation of Special Achievement.

Berg Chairs NCHGR Committee

Stanford biochemist and molecular biologist Dr. Paul Berg has been named the new chair of the program advisory committee on the human genome for the National Center for Human Genome Research. He succeeds Dr. Norton D. Zinder of Rockefeller University.

Berg is joined on the committee by two other new members, Drs. Diane Smith and Robert Tjian. The new members will serve 4-year terms.

Berg is currently director of the Beckman Center for Molecular and Genetic Medicine in Palo Alto, Calif., and professor of biochemistry at Stanford University School of Medicine. He received the Albert Lasker Basic Medical Research Award and the Nobel Prize in chemistry in 1980 and also coauthored the recently published reference text Genes and Genomes.

Smith is an engineer and mathematician who has been working in the field of computer science since 1972. She spent the first 5 years of her career on the computer science faculty at the University of Utah. After leaving the university to join the Computer Corporation of America, she became vice president for advanced information technology. She is currently the manager of technology development for the custom systems division of Xerox Corp.

Tjian has broad experience in the areas of molecular and cellular biology with a specific focus in the field of virology and regulation of gene transcription. He has been an investigator at Howard Hughes Institute since 1987 and a professor in the department of biochemistry, University of California at Berkeley, since 1982. His awards include the Pfizer Award for Enzymology in 1983 and the Milken Family Medical Foundation Cancer Research Award in 1988.
EGAD
(Continued from Page 1)

committee should evaluate which application is an administrative nightmare.

Feldmann, with a reputation as a free-thinking problem solver, and Mathis, an experienced grants administrator, began to tackle the routing problem by assembling a chart that cross-referenced 107 research grant subject areas with the 96 study sections that evaluate proposals. The chart would allow Mathis and Feldmann to develop a formal procedure to determine what types of grant applications should go to which study sections.

Distilling the information and bringing it together into one chart was a revolution in itself, according to Feldmann. It was an early step in modernizing a process that had been in place, mostly unchanged, since the end of World War II, and the first step in bringing modern computing power to bear on a process carried out largely on paper.

With chart in hand, Feldmann wrote an experimental computer program that DRG referral officers could use to assign incoming applications to the study sections having the appropriate expertise. At that time, however, the application information that the referral officers needed to make their decisions was still on paper. To use Feldmann's program these officials had to read the application and select key words from a term list, an efficient process, but not much of a time-saver.

Even though this first effort was not a complete success, the collaborators were excited about their progress and continued to work together. As he became more familiar with the way DRG handled data and made decisions, Feldmann recognized other ways that computers could be used to streamline the application process. At the time, applications were being entered into a computer, printed on paper, sent to the next person in the review process, reentered into a computer, printed on paper, etc.—at an enormous cost of energy and time.

This repetition meant that it took 11 months from the time a researcher began writing a grant application to the time he or she received an answer about funding from NIH. Feldmann and Mathis decided that if applications could be created, submitted, routed, reviewed, and returned, all the while keeping the data on the computer, scientists could know the status of their application in half the time.

Computerizing the 40-year-old NIH grant process was an ambitious proposal, and many people comfortable with the old system were wary of turning the status quo upside down. As Feldmann and Mathis began explaining their ideas, however, apprehension began to erode. With Feldmann's creativity and Mathis' knowledge of the grant process, the two were confident they could gain the acceptance of the research community and NIH officials.

Their EGAD project was touted in the Apr. 29, 1991, issue of Nature as the "Grail of grantmaking," a long-needed solution to a number of problems that plague all government granting agencies. Nature credited the project's beginnings to "a handful of computer evangelists with some hot machines," a characterization that amuses Feldmann. "It was just me and John," he says.

The first EGAD prototype took Feldmann a month to write, borrowing some ideas from an earlier NSF attempt at electronic grant applications and the IRS electronic tax return project. The prototype surprised even his collaborator. "Feldmann’s computer program was a stunning kick in the pants," according to Mathis. "It showed that it could be done."

Once they had the prototype, the collaborators wanted to know if the research community would accept it. A thousand copies of the program were sent out to scientists around the country, and their comments and feedback were used to refine the program.

Today, Mathis is the chief advocate for the EGAD project that begins field trials this fall. As Feldmann devotes his time to multiple collaborations, Mathis is building support for EGAD among the on-campus ICDS and the extramural community. A computer contractor is honing the PC and Mac versions of the program before the field trials begin.

The innovative collaboration that led to EGAD is not unusual for Feldmann, who is in the business of developing novel approaches to seemingly impossible problems. He frequently receives calls from researchers in the intramural and the extramural communities. They call with what they feel are insurmountable difficulties and Feldmann replies, "Don't worry about that, just bring your data; you have the content knowledge, I'll build the model." After speaking with them, he looks for a way to utilize DCRT's computing resources to build a model or develop a new solution.

In the case of EGAD, Mathis brought his years of technical expertise on the administration of the grant process to Feldmann, who asked some tough questions and then exploded with ideas. Retrospectively, Feldmann explains their continuing collaboration this way: "The problems that John and I can solve, we do; those that we can't solve, we solve recursively—we keep coming back to them until we do solve them."

As the EGAD project continues to develop, the enormity of its potential impact on the future of grantmaking becomes more apparent. EGAD will change the way that researchers think about the grant application process, and it could lead to a universal electronic grant application to be used by other government funding agencies. That is a lot to come out of the initial conversation Mathis and Feldmann had 4 years ago. "Every time we turned a corner on this project it exploded," says Mathis. "It went up an order of magnitude. It has certainly helped that Richard has an unfettered way of thinking about problems."

Feldmann has no doubts about the future of EGAD. "Once you find the right idea," he proclaims, "the transformation is inevitable."
Strausberg Heads NCHGR Technology Development Program

Even though advances in recombinant DNA technology have enabled researchers to make amazing strides in biomedical research during the last 20 years, more technological advances will be necessary to map and sequence the human genome efficiently. Current technologies work reasonably well when researchers focus on a small area of the genome (part of a chromosome, for instance) but are expensive and labor intensive. Consequently, new technologies to accomplish rapid large-scale mapping and sequencing must be conceived and developed.

Leading NCHGR’s search for new technologies is Dr. Robert L. Strausberg who recently joined the center staff from Genex Corp., a biotechnology firm in Gaithersburg. His task is to champion promising research proposals and to coordinate the center’s burgeoning technology development program. As assistant to the director for technology development, he will ensure that critical areas of technology development necessary to accomplish NCHGR’s goals are addressed. He will also act as an advocate for researchers with unique and exciting ideas for new technologies and will foster the integration of these technologies into an overall research plan.

In his additional role as director of the Technology Development Program, Strausberg will also be responsible for the management of grants to develop cost-effective large-scale sequencing of DNA, focusing on bringing down the cost. He will also manage the grant programs for new technology developed through the R01, R21 (exploratory/developmental grants) and SBIR (small business innovative research) funding mechanisms. He will encourage multidisciplinary collaboration within large research projects and will organize workshops and working groups for those interested in particular areas of technology development.

Strausberg also anticipates advising researchers at universities and in industry about how to participate in the human genome project. He plans to elicit suggestions from individuals on ways NCHGR can be more helpful in facilitating their research efforts. “Even if they currently have no background data, no track record, etc., I’m still eager to talk with those researchers who have novel ideas for large-scale sequencing and mapping. NCHGR wants to encourage innovation and fund projects with potential.”

Strausberg’s selection for this position ended a nationwide search for a candidate with a broad perspective gleaned from experience in both academia and the biotechnology industry. After receiving his Ph.D. in developmental biology from Ohio State in 1976, he went on to a postdoctoral fellowship in biochemistry at Northwestern Medical School in Dallas. From 1979 to 1982, he served as assistant professor of biology at Southern Methodist University in Dallas, where his research focused on yeast molecular biology. In 1982, he joined Genex as principal research scientist, eventually attaining the position of senior director of research responsible for DNA sequencing, DNA synthesis, cDNA and genomic cloning, and expression of foreign genes in yeast and E. coli.

Study Requires Boys

The Child Psychiatry Branch, NIMH, is recruiting boys between the ages of 6 and 12 who have the dual diagnosis of Tourette syndrome and attention deficit hyperactivity disorder. Call Gail Ritchie, 496-0851.

Ex-NIDDK Investigator Honored

Dr. Richard Rothman, formerly of NIDDK’s Laboratory of Medicinal Chemistry, was recently selected for the 1991 Joseph Cochin Young Investigator Award by the committee on problems of drug dependence. The award recognizes Rothman’s contributions to opioid pharmacology research as a member of the NIDDK lab, including studies of the mu and delta binding sites of an opioid receptor complex and a mathematically based method for designing and analyzing ligand binding data. Rothman has also contributed to understanding the physiologic mechanisms involved in developing tolerance and dependence for morphine.

Most recently, Rothman and his collaborators have been developing and investigating drugs that may counter the effects of cocaine. They published data last year suggesting that certain high affinity dopamine reuptake inhibitors might antagonize cocaine’s neurochemical effects. This research follows Rothman’s studies of cyclofoxy, an opiate antagonist that is now used in studies on conscious humans to image opioid receptors.

Originally formed by the National Research Council of the National Academy of Sciences, the committee on problems of drug dependence is today an independent research organization sponsored by major scientific associations, including the American Medical Association and the American Chemical Society. As a public service, the committee informs researchers in pharmaceutical, governmental and academic laboratories of the physical dependence potential and abuse liability of new analgesics, stimulants and depressants. Among the federal agencies that use the information from these studies are the Drug Enforcement Administration and the Food and Drug Administration.

Rothman recently joined the Addiction Research Center of the National Institute on Drug Abuse.
CANCER
(Continued from Page 1)

"This did not translate into a survival advantage," Broder said, referring to an NCI study in which two-thirds of throat cancer patients' larynxes were spared, "but I submit to you that the ability to speak is astonishingly important. It defines who an individual is in his or her own life and therefore the loss of that function is certainly not trivial and the preservation of that function is a major advance."

These 'neo-adjuvant' therapies are very important, Broder said, but what is equally important is maintaining a balance between celebrating hurdles overcome and confronting challenges yet to come.

Cancer researchers must continually remind themselves, he said, of the question Congress asks him annually: What has been done with the people's $20 billion? That is the amount the nation has committed to the national cancer program since the early 1970's when President Nixon signed the 1971 National Cancer Act and the program was redefined, between 1970 and 1973, in its current form.

"In effect we have a mixed review," Broder said, comparing 1973's data on cancer incidence and death with 1988 information. "With some cancers we must categorically say that things have gone the wrong way."

For example, lung cancer in women has increased more than 100 percent in both incidence and death rate.

"For most cancers," Broder asserted, "incidence drives mortality. And that's a glorified way of saying prevention has to be our first priority."

Melanoma of the skin, multiple myeloma, non-Hodgkin's lymphoma, lung cancer in men, and prostate cancer have also risen in incidence and death in the last two decades. A look at all cancers shows a 15 percent increase in incidence and a 5 percent increase in death rate since 1973.

"You can put whatever spin you want on this information," Broder said, "but my position is we need to do better."

Better rates were seen for other common cancers. For instance, significant reductions in incidence and death rate have been realized for diagnoses of Hodgkin's disease, colorectal and bladder cancers as well as for such gynecological malignancies as the ovaries, uterus and cervix. The 25 percent drop in ovarian cancer in women under age 65 can be directly traced to a number of NCI accomplishments—for example, better staging, or diagnosing, and more effective use of combination chemotherapy, he said. Also, the 50 percent reduction in the death rate of Hodgkin's patients, Broder noted, is largely attributable to work done in the Clinical Center.

"There are clearly some areas in which we have made progress and in many cases they clearly are due to technologies developed by the national cancer program," Broder acknowledged.

He further cited unexplained reductions in gastric cancers, which have declined worldwide. Possible plausible reasons for the falling rates include dietary changes that range from declines in the population's salt and nitrite intake to an increasing, trans-seasonal availability of key nutrients found in fresh fruits and vegetables. One well-worn explanation Broder would not accept, however.

"For those of you who persist in the refrigeration theory," he quipped, "please be advised: Refrigerators had been invented in 1973."

Acknowledging the success of scientists who believe passionately in the potency of cancer treatment, Broder noted that the death rate of testicular cancer has dropped sharply, even though the incidence has increased slightly.

"This is the signature for progress from a treatment point of view," he said. "There have been extremely brilliant advances in the treatment of testicular cancer."

Categorized by age, advances in cancer research are mainly encouraging for the population under age 65. Lung cancer deaths and incidence, especially in women, significantly skew the statistics, raising the average death rates and incidences for all other cancers. The lung cancer death rate for women under 65 shows about a 70 percent change from 1973 to 1988.

Although Broder said he wanted to emphasize the importance of scientists advocating prevention, he also wanted to caution them not to blame the public they serve.

"Everyone knows that you can prevent lung cancer to a very large extent by smoking intervention studies and we should do that," he urged. "But a corollary to that should not be that we say, 'Don't blame us. If people didn't smoke they wouldn't die of lung cancer.'"

"Part of our job is to be more effective at getting people to stop smoking," he continued. "To develop better ways of diagnosing and treating lung cancer, though, we're going to have to go back to the lab and keep working. But don't blame the consumer."

Broder said most beneficiaries of advances against cancer are under age 50. Perhaps it was to be expected, he noted, that those who benefit first from new ideas and knowledge are those who are the youngest, and have the most to gain from changes of lifestyle, changes in diet and changes in medical practice.

Comparison of the cancer incidence and death rates of whites to those of the minority population revealed sober facts. In breast cancer, for instance, the death rate for white women has dropped about 13 percent. In fact, the rates have dropped for all ages of white women under age 60. In contrast, there has been no progress in any age group for Black women. Broder said this statistic, like those contrasting young and older age groups, may reflect the effect that access to cancer prevention, diagnosis and treatment programs has on death rates from the disease.

"For Black individuals in this country—and I believe the racial designation here is probably a surrogate marker for poverty—there are a number of common tumors for which the ratio of incidence and death is extremely unfavorable," he said. "Poverty is a carcinogen."

Broder also compared rates for non-Hodgkin's lymphoma to Hodgkin's disease. Non-Hodgkin's affects about 40,000 Americans and has risen in incidence and death rate in the 10-year period between 1976 and 1986. The disease shows no sign of abatement either, Broder said. The rates for Hodgkin's disease have not changed over the same interval, even though enormous strides—curative therapies in some settings—have been made in NCI clinical research on the disorder.

"Something is wrong," Broder said. "We have not been able to translate this into a public health advance. We cannot convince the public—or the Congress, which in this case represents the public—that we have made progress against a disease when the incidence and death rates are going up."

Looking to future developments, the director of the country's largest cancer research program admitted to endorsing the possibility of immunizing against cancer.

"Prevention has to be our first priority," Broder reiterated. "I am strongly committed to the principle of vaccine development."

He also briefly mentioned several promising but unexpected windfalls in cancer research including the development of the revolutionary polymerase chain reaction diagnostic test and the controversial Pacific yew tree bark treatment for ovarian and breast malignancies.

"The problem here," Broder said, referring to the ecological conflict over evicting spotted owls, who reside in the yew trees, to extract the experimental cancer drug taxol from the tree bark, "is that we are dealing with an example of a finite supply of a drug. We are confronted with an extreme shortage of this drug."

About 4,000 female cancer patients could be treated with the amount of taxol now available in the best circumstances, Broder said, but at least 12 times that amount—50,000 women facing death from refractory ovarian or breast cancer—could make reasonable arguments for the drug.

Broder concluded his state of the science address by urging researchers to "stick to the facts of the story as we have them. There are a number of areas where we can be very proud and very optimistic."

Earlier in his presentation, Broder had
shown a slide comparing the progress rate against the number one killer in the United States—heart disease—and the progress rate against the runner-up, cancer, in people under age 65. A plunging cardiovascular slope—indicating the dramatic decline in heart disease deaths—was drawn on the same graph as an only slightly falling cancer curve.

"Professor Claude Lenfant (NHBLI director) has a significantly better curve to look at," Broder said, grinning. "What I urge you to do is give me or the next director of NCI this kind of curve. I don't care how you do it. You asked for advice—This is what I want."

Free Family Portraits Offered

As part of its effort to enhance employee benefits, R&W is offering members a free 10x13 family portrait on canvas. Executive Color Studios will be on campus Friday, Sept. 20 through Sunday, Sept. 22. Sittings will take place in the Little Theater in Bldg. 10, part of the Visitor Information Center. Appointments can be scheduled by calling 1-800-227-5664 between Aug. 7-21.

Members may purchase additional portraits in various sizes, but there is no obligation. For more information call R&W, 496-6061.

TRAINING TIPS

The NIH Training Center of the Division of Personnel Management offers the following:

<table>
<thead>
<tr>
<th>Courses and Programs</th>
<th>Starting Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management and Supervisory</td>
<td>496-6371</td>
</tr>
<tr>
<td>Communications for Results (Phase II)</td>
<td>7/30</td>
</tr>
<tr>
<td>Time Management</td>
<td>8/3</td>
</tr>
<tr>
<td>Reviewing Other People's Writing</td>
<td>8/7</td>
</tr>
<tr>
<td>Recognition Secrets: Innovations for</td>
<td></td>
</tr>
<tr>
<td>Rewarding Today's Workers</td>
<td>8/8</td>
</tr>
<tr>
<td>Practical Management Approaches</td>
<td>8/8</td>
</tr>
<tr>
<td>Using Animals in In Vitro Research:</td>
<td>9/5</td>
</tr>
<tr>
<td>Guidelines for Investigators</td>
<td>9/9</td>
</tr>
<tr>
<td>Voice for Success</td>
<td>9/17</td>
</tr>
<tr>
<td>Effective Communications (Phase I)</td>
<td></td>
</tr>
<tr>
<td>Office Operations and Administrative System Training</td>
<td>496-6211</td>
</tr>
<tr>
<td>Quality Writing I</td>
<td>7/29</td>
</tr>
<tr>
<td>Reducing Stress: Rebuilding Energy for</td>
<td></td>
</tr>
<tr>
<td>Office Support Personnel</td>
<td>7/30</td>
</tr>
<tr>
<td>Special Courses 496-6211</td>
<td></td>
</tr>
<tr>
<td>Basic Employee Relations</td>
<td>9/11</td>
</tr>
<tr>
<td>Basic Labor Relations</td>
<td>8/19</td>
</tr>
<tr>
<td>KSA Methodology Training</td>
<td>8/19</td>
</tr>
<tr>
<td>American Sign Language Level 1</td>
<td>9/10</td>
</tr>
<tr>
<td>American Sign Language Level 2</td>
<td>9/10</td>
</tr>
</tbody>
</table>

Personal Computer training is available through User Resources Center (URC) self-study courses. There is no cost to NIH employees for these hands-on sessions.

The URC hours are:

- Mon. — Thurs: 8:30 a.m. — 7 p.m.
- Friday: 8:30 a.m. — 4:30 p.m.
- Saturday: 9 a.m. — 1 p.m.

The NIH Training Center, DCRT, and other training information is available on WYLBUR. Logon to WYLBUR and type ENTER TRAINING.

Dr. Artrice Bader Retires After 32 Years of Government Service

Dr. Artrice V. Bader, a program administrator in the Cellular and Molecular Basis of Disease (CMBD) Program of the National Institute of General Medical Sciences, has retired after 32 years at NIH.

She began her NIH career in 1957 as a biologist in the National Heart Institute. In 1961, she transferred to the National Cancer Institute as an electron microscopist in the Special Virus Leukemia Program. During that time, she attended George Washington University at night, working toward a master of science degree, which she received in May 1963. In the fall of 1963, Bader began full-time studies at Georgetown University, and in 1966 she became the first Ph.D. recipient from the school's biology department.

She returned to NIH in July 1966 as a staff fellow and later became a research biologist in the institute's Virology Program. As a cell biologist with a specialty in electron microscopy, she was involved in studies of RNA tumor viruses.

In 1976, Bader joined the NIGMS Generics Program to administer grants in the areas of protein synthesis and translation and other aspects of gene regulation. In 1978, she transferred to the CMBD program, where she administered a portfolio of grants in cell organization, motility and division.

Among her honors are four NIGMS performance awards, a special commendation from the NIGMS director, inclusion in Outstanding Young Women of America, and election to the Beta Kappa Chi and Alpha Kappa Mu honor societies. Bader is a member of the American Society for Cell Biology, the American Association for the Advancement of Science, and the NIH Alumni Association.

Married to NCI scientist Dr. John Bader, she is the mother of two children and two stepchildren. During retirement, she plans to enjoy her family while working as a consultant in science management and review.—Wanda Wardwell

Dr. Claude Lenfant (rear, second from r), NHLBI director, honored bone marrow donors (clockwise from top l) Fernando Gaitan, Maria Gaitan-Andres, Robin Williams and David Lanier, and recipient Celine Larochelle at a recent institute workshop on minority bone marrow donor recruitment. Larochelle and the four marrow donors were given certificates of appreciation for their participation in an NHLBI marrow donor recruitment video targeted at minorities. The workshop, part of the institute's program to assist marrow donor centers in recruiting more minority donors, provided training for coordinators from 14 marrow donor centers, including the NIH Center, and staff of the National Marrow Donor Program in St. Paul, Minn.
New Rehabilitation Medicine Center Joins NIH

NIH's family has officially expanded: The agency's newest entity, the National Center for Medical Rehabilitation Research (NCMRR), established within the National Institute of Child Health and Human Development, was announced July 9.

The product of congressional legislation signed into law last November by President Bush, NCMRR will conduct and support research to develop techniques and devices for medical rehabilitation to improve the quality of life and increase the independence of the 35 million Americans with disabilities.

One of the center’s priorities will be to support research leading to improved technologies and techniques to reactivate muscle, nerves and bodily functions impaired by injury, disease, disorder or birth defect, and to improve prosthetic devices.

NCMRR also has responsibility for supporting research training programs and for disseminating health information. It will eventually include an intramural component conducting both basic sciences research and clinical studies.

DHHS secretary Dr. Louis Sullivan, who announced creation of NCMRR, said, "The new center will conduct and support the work of engineers and scientists seeking to restore, replace and enhance the function of children and adults with physical disabilities."

The center is the fourth national center to join the 13 institutes, three divisions, Clinical Center, Fogarty International Center, and National Library of Medicine that constitute NIH.

NICHD director Dr. Duane Alexander, who is acting director of the center, said, "Rehabilitation medicine and associated therapies may soon be able to use findings from basic research to improve or replace the loss of central nervous system function, and impairment resulting from arthritis, cardiovascular disorders and other functional limitations.

"In the future, we look forward to applying the advances in microcomputer hardware and software to externally control implanted devices to regulate a variety of body functions including opening and shutting anal and urinary sphincters, releasing drugs and hormones, and sequencing or modulating neural impulses to muscle groups." 

NOF Honors Healy, Two Institute Directors

The National Osteoporosis Foundation (NOF) recently presented special recognition awards to NIH leaders at its annual awards luncheon on Capitol Hill.

Honored were NIH director Dr. Bernadine Healy, NIAAMS director Dr. Lawrence E. Shulman and NIA director Dr. T. Franklin Williams, who is leaving NIH this summer to return to the University of Rochester.

The awards were presented by Paul Rogers, a former congressman who now chairs the NOF board of trustees. He cited Healy's new women's health initiative, to be sponsored by NIH: "In this one announcement, Dr. Healy has focused enormous attention on the link between women and osteoporosis and the serious consequences of osteoporosis on the quality of life for all women."

Presenting the award to Shulman, Rogers mentioned the fifth anniversary of NIAAMS, which is the lead agency for research on osteoporosis, and congratulated the director for his own research on the disease.

Rogers recognized the upcoming departure of Williams from NIH and praised his leadership in fostering research on the aging processes and problems of older people.

NIGMS Scientist Joins American Delegation to African Summit

Dr. Yvonne Maddox, deputy director of the NIGMS Biophysics and Physiological Sciences Program Branch, was among the participants in the African/African American Summit, a meeting held recently in Abidjan, Cote d'Ivoire, West Africa.

The meeting is the first time that leaders from over 25 African countries have met with major African-American leaders who represent civil rights organizations, religious groups, the government, academia and industry. American participants included Rep. William Gray, III, the House majority whip; Rep. Mervyn M. Dymally, a member of the House Foreign Affairs Subcommittee on Africa; NAACP executive director Dr. Benjamin Hooks; and

Mrs. Coretta Scott King. The purpose of the summit was to propose plans to assist with the educational, industrial, agricultural, medical, and economic development of Africa, as well as to set strategies for creating closer cooperation between Africans and African Americans for the support of African nations.

Maddox attended as the chair of the board of directors of the Center for Development and Population Activities.

The 3-day meeting included workshops and seminars in which the more than 500 participants discussed a variety of issues.

The historic conference ended with a commitment to strengthen ties between the U.S. and Africa through efforts to increase American foreign aid to the region and to relieve African nations of their $100 billion debt.