From Natural Products, New Drug Discoveries

By Belle Waring

This is a true-adventure story spanning the globe, over land and sea. This is a modern quest with many heroes—and heroines—fanning out like spokes on a wheel, with its hub at NCI in Frederick. That’s where you’ll find a program unique in government, representing a trend that’s not confined to one IC or a single study.

“Our mission is not basic research: It is to find, develop and get out the drugs,” says Dr. David Newman, chief of NCI’s Natural Products Branch (NPB).

“We’re part of what we can call Uncle Sam’s non-profit pharmaceutical house, and our job is to find leads to compounds that ameliorate cancer.”

Tucked inside Ft. Detrick, an active U.S. Army base, NPB brings in raw materials from terrestrial and marine environments worldwide to be held in its Frederick repository. Samples are then

Church Volunteers From 1954-1975 Reunite at Clinical Center

By Jenny Haliski

Eating only lima beans. Sleeping with weights on your eyes. Drinking a mixture of corn oil and skim milk. It might seem strange now, but these were some of the diets that a group of Mennonites and Church of the Brethren members who served as healthy volunteers consumed while participating in clinical research studies at the Clinical Center from 1954 to 1975. About 25 volunteers, together with their family members, reunited recently at the CC and traced how their contributions decades ago changed the course of clinical research for the better.

The reunion, spearheaded by Dr. Jim Conrad, a member of the Mennonite Church from Perkasie, Pa., offered a chance for the group to reflect on their experiences as “creatures made in the image of God [who] need to express God’s love by how we live our lives.” For these faith communities, service to those who are ill exemplifies “another way of living.” Both

Graduate Student Research Festival Gives Early Look At NIH Training

For 2 days in October, graduate students from across the country had the opportunity to learn what it might be like to conduct research at NIH. The National Graduate Student Research Festival gave attendees the chance to present research to an audience of peers and NIH scientists, explore opportunities for postdoctoral training, learn more about approaches to research here, network with NIH fellows and investigators and, for many, see the NIH campus for the first time.

“It’s a great opportunity for people in the position we’re in now, who haven’t even defended a thesis yet” to learn more about
Three NIH Scientists Named AAAS Fellows

Three NIH scientists have been awarded the distinction of AAAS fellow; election is an honor bestowed upon members of the American Association for the Advancement of Science by their peers. They join a class of 471 new members announced Oct. 26 in Science.

Honored because of their scientifically or socially distinguished efforts to advance science or its applications are: NIGMS director Dr. Jeremy Berg, from the section on chemistry, who was cited for distinguished contributions to the structure and functions of metal ions in proteins and for leadership in advancing research in service to humanity; and two scientists from the section on the medical sciences—NCI director Dr. John Niederhuber and NCI’s Dr. Mark Udey.

Niederhuber was elected for pioneering research on MHC (major histocompatibility complex) immunology and cancer stem cells and outstanding leadership of the University of Wisconsin Cancer Center and NCI. Udey was recognized for seminal research on the biology of Langerhans cells (epidermal dendritic cells) and the role of E-cadherin and TGF-beta in their development and localization.

The tradition of AAAS fellows began in 1874. AAAS, founded in 1848, is the world’s largest general scientific society.

BIG Helps Recruit Marrow Donors

The NIH chapter of Blacks in Government and the NIH Marrow Donor Program recently sponsored an effort to recruit volunteers for the National Bone Marrow Registry (NBMR). The program “Do Something Good” informed the NIH community about life-threatening blood diseases and genetic disorders. The session also invited NIH’ers to become life-saving volunteers.

Diseases that afflict minorities include leukemia, aplastic anemia and sickle cell anemia. Because African Americans and other minorities have unique genetic backgrounds, it is often difficult to find a donor with bone marrow that matches the genetic makeup of these patients. An estimated 70 percent of minorities will not find a match within their families.

A highlight of the program was testimony given by an NIH family that benefitted from NBMR. An NIDDK employee’s son was saved by transplants from donors on file at the registry (see NIH Record, Sept. 8, 2006). For details on the NIH Marrow Donor Program, contact Earl Simmons, (301) 435-4365, or Gina Boyd, (301) 496-0572.

Wyatt Receives Surgeon General’s Highest Honor

Dr. Richard G. Wyatt (r), deputy director of the Office of Intramural Research, was awarded the Surgeon General’s Medal in recognition of seminal research on the biology of Langerhans cells (epidermal dendritic cells) and the role of E-cadherin and TGF-beta in their development and localization. The honor recognizes Wyatt’s 36 years in the Commissioned Corps, from which he retired on Sept. 1. He will continue in his OIR post; he has served that office since 1984.

ORS Updates Emergency Procedures

The Office of Research Services recently updated its emergency procedures for NIH personnel. Advice is offered on conditions including: reporting suspicious persons or activities, lockdown situations, suspicious packages or objects, bomb threats, evacuations, fire emergencies and threatening/violent behavior. To review the guidance, visit http://ser.ors.od.nih.gov/documents/EmerProcPersonnel.doc.

PRAT Program Accepts Applications

The NIGMS Pharmacology Research Associate (PRAT) program is now accepting applications for positions to begin October 2008. This competitive research fellowship program supports training at NIH or FDA laboratories for postdoctoral candidates. It focuses on the pharmacological sciences and related research areas such as molecular pharmacology, signal-transduction mechanisms, drug metabolism, immunopharmacology, chemistry and drug design, structural biology, endocrinology, bioinformatics and neuroscience.

PRAT fellowships are 3-year appointments at competitive salaries; some supply and travel funds are provided to help support research in preceptors’ laboratories. Applicants must identify a preceptor in their application. Preceptors may be any tenured or tenure-track scientist at NIH or FDA who has agreed to host the applicant. Applicants must be citizens or permanent residents of the U.S. and have been at NIH or FDA for no more than 1 year at the time they submit their application. Applications for the 2008 PRAT Fellowships will be accepted up to Jan. 30, 2008. For more information or application materials, contact the PRAT program assistant at (301) 594-3583 or email prat@nigms.nih.gov.
NIBIB, India Partner to Develop Low-Cost Medical Technologies

In a ceremony held Oct. 5 in New Delhi, India, NIBIB and the department of biotechnology (DBT) of the Ministry of Science and Technology, Republic of India, signed a bilateral agreement to develop low-cost health care technologies aimed at the medically underserved. Participants in the signing ceremony, held during the Indo-U.S. meeting on translational health sciences, were NIBIB director Dr. Roderic Pettigrew and DBT secretary Dr. Maharaj Bhan.

The agreement is based on a shared commitment to improve the health and well-being of the people of both countries by encouraging collaborations and cooperation on the development of diagnostic and therapeutic medical technologies that are inexpensive and operate at the initial point of physician contact, or point of care.

Areas of cooperation outlined in the agreement include low-cost innovations in X-ray technology; nanotechnology-based biosensors; point-of-care diagnostic technologies; telehealth and telecommunication technologies; and neonatal health technologies. The disease areas and conditions likely to be affected by the successful development of the technologies are infectious diseases, cardiovascular disease, liver disease, trauma and injury and conditions associated with infant mortality.

“We are very pleased to officially establish this groundbreaking effort between NIBIB and DBT,” Pettigrew said. “This agreement will create a working partnership designed to help address global health disparities by encouraging the development of improved methods and technologies to diagnose and treat illness and injury across geographic and economic borders.”

DBT’s Bhan noted, “Developing low-cost health technologies that are unique in design to be affordable and useable in disease prevention and management is a high priority in India. The partnership with NIH, and through them, with U.S. institutions, is critical for us to make progress. We are excited about this agreement with NIH to bring multiple disciplines and teams together to find innovative solutions.”

As part of the agreement, NIBIB and DBT will encourage workshops and meetings to share experiences and scientific information; link appropriate centers of excellence and institutes; engage in bilateral cooperation on the assessment and application of new diagnostic technologies; and generate collaboration among scientists and engineers in the conduct of research, research training and technology development. The agencies will facilitate and share each other’s efforts in research and development through regular interactions between scientists, and will work towards mutual, annual goals.

India’s Dr. Maharaj Bhan (l) and NIBIB director Dr. Roderic Pettigrew shake hands following the signing of the bilateral agreement. Witnessing the occasion are (from l) Steven White, deputy chief of mission, U.S. Embassy, New Delhi; NIH director Dr. Elias Zerhouni; Kapil Sibal, science minister; T.S. Rao, medical biotechnology group leader; and FIC director Dr. Roger Glass.

NHLBI Group Finishes Marine Corps Marathon

NHLBI employees (from l) Chris Olaes, Darci Phillips, Angel Aponte, Stefanie Marques and Joni Taylor ran and finished the Marine Corps Marathon on Oct. 28. For Phillips, who recently ran the Boston Marathon, this was her second Marine Corps Marathon. It was the first marathon experience for the others.
groups are recognized peace churches affiliated with the National Service Board for Religious Objectors, now the Center on Conscience & War.

One volunteer recounted how his mother often told him, “Someday you’ll serve your country in the Brethren Volunteer Service (BVS) instead of the military.” Local draft boards accepted boys’ participation in public service projects in lieu of military service. Girls from both churches generally contributed 1 or 2 years to youth service activities such as medical or social work.

CC director Dr. John Gallin noted that, like many of the researchers in his generation who joined the Public Health Service, healthy Mennonite and Brethren volunteers also share a commitment to “save life and not destroy it,” to quote President Franklin D. Roosevelt’s 1940 NIH dedication speech. Although many came to the PHS during the Vietnam War from 1959 to 1975, the Mennonite and Brethren volunteers came to NIH as early as the Korean War in 1954.

Mandy Jawara of the CC Office of Patient Recruitment & Public Liaison updated the group on the Clinical Research Volunteer Program, which began in 1954 as a collaboration between NIH and the Mennonite and Brethren church’s service agencies, which in turn formed their own volunteer services. Until 2006, 50 to 100 students a year came to live at the CC while participating in clinical research and earning academic credit for their service. Jawara, who coordinates the program, said that although it has changed—healthy volunteer students no longer live on the patient care units—its mission of providing assistance to ICs whose research involves healthy volunteers remains the same.

In his welcome to the group, Gallin described the numerous medical advances from CC history—none of which would have been possible without healthy volunteers’ participation as control subjects. “We will never be able to thank you appropriately. Your contributions to society have been enormous,” he said.

Joyce Bohn displays a 1957 Washington Post article describing her experience as a healthy volunteer at NIH. Bohn, who came from a family of 10 children and couldn’t afford college, was one of several in the group who received a year of tuition at American University in exchange for service as a healthy control subject. She bonded so closely with her roommate, an osteoporosis patient, that the roommate loaned Bohn all of her university expenses without interest so she could continue her studies and the two friends would not be separated. Taking the roommate up on her offer, Bohn met her husband at the Church of the Brethren’s Bridgewater College. “My life changed tremendously because of NIH,” she said, wiping away tears.

Dr. Allan Mirsky of NIMH and Dr. Robert Shamburek of NHLBI gave presentations on the clinical impact of the group’s assistance on mental and cardiac health research.

According to Mirsky, many volunteers helped NIMH researchers standardize tests of attention, in part by participating in a 1956 study that has been cited in the literature more than 1,000 times and led to development of the continuous performance test (CPT). Thanks to these control patients, NIMH researchers also compared psychological test performance in seizure-disorder patients; described behavioral effects of the first effective anti-psychotic drugs used to treat schizophrenia; contrasted behavioral and physiological effects of anti-psychotic drugs and sedatives; and described effects of stimulant drugs in healthy volunteers through
sleep deprivation studies. Mirsky reminisced about coming to campus in the middle of the night to play billiards with a BVS volunteer who hadn’t slept for 70 hours. “She couldn’t do a CPT, but she could complete more challenging tests, including beating me at pool!”

The Amish and Mennonite populations have the highest percentage of a rare genetic disorder called sitosterolemia, in which plant cholesterol becomes extremely high because the body is unable to excrete it into the bile for removal from the body. By observing volunteers from these communities, researchers developed drugs to block cholesterol’s absorption in the intestines; the drugs are now used in millions of patients with ordinary cholesterol disorders.

Marian Payne, a normal volunteer in 1956 who returned to the CC in the late 1990s as a sitosterolemia patient and participated in investigational treatments, said that if it wasn’t for NIH’s research, “I wouldn’t be here today or be in the health I enjoy today.”

Shamburek also unearthed hundreds of historic documents to show the group, including media coverage from the time, much of which brought exclamations from his audience as several people recognized themselves.

After tours of the CRC, the group reconvened to tell stories of their experiences and pore over photos and articles. The recollections shared a common theme: how much the volunteers’ lives changed as a result of coming to the CC. Carson Good discovered social work, which became his career. Two couples in the group—Marilyn and Dave Verbeck and George and Judy Reimer—met at the CC and married shortly thereafter.

The volunteers—all of whom were 18 or older, many of them away from their rural communities for the first time when they came to NIH—especially appreciated the exposure to diverse cultures in the Washington area. In their free time they went to Washington Senators baseball games, boated on the Potomac or attended concerts and sporting events. One participant said, “The culture and social learning we received while at NIH molded our lives to this very day.”

Back by Popular Demand
Management Seminar Series Begins Second Year

Last year’s DDM (Deputy Director for Management) Seminar Series provided audiences with dynamic presentations on topics ranging from change management to leadership strategy. The series was a success—more than 900 NIH employees attended.

This year, audiences can look forward to more presentations with the launch of the second annual series, “Management & Science: Partnering for Excellence.” With four seminars in all, this year’s events focus on topics such as: managing across generations, undergoing change, personal accountability and workforce diversity. These issues are especially pertinent as NIH becomes a more diverse workplace.

The opening seminar features Lynne Lancaster and David Stillman on Thursday, Nov. 29 from 11 a.m. to 12:30 p.m. in Masur Auditorium, Bldg. 10. Drawing on audience participation and reaction, the speakers will make their presentation, titled “What a Difference a Generation Makes,” educational for all who attend.

Lancaster is a writer and communications consultant born in the Baby Boomer generation. Stillman is an entrepreneurial “Generation X’er,” internationally known for his former career as a radio and TV reporter and for receiving a CLIO Award. Together they’ve written When Generations Collide: Who They Are. Why They Clash. How to Solve the Generational Puzzle at Work, a look at the interplay between the four generations that currently share the conference table.

Future speakers include Dr. Al Siebert (Feb. 14), Jim Sorenson (Apr. 17) and Dr. Samuel Betances (June 12). The 2008 seminars are scheduled for 11 a.m. to noon in Masur Auditorium.

Sign language will be provided and each seminar will be videocast. For more information visit www.ddmseries.od.nih.gov/ or call (301) 496-3271.

Alert Response Minimizes Water Damage to NLM Collections

On Oct. 3, a burst hose in a water filtration unit in NLM’s Book Repair Lab (filtered water is required for use in rare book conservation work) soaked the lab floor and some materials. NLM employees Jim Labosier and Sandy Taylor promptly reported the problem and draped plastic over collection materials. Water found its way through the floor, but fortunately landed on audiovisual cassettes in closed plastic cases that could be wiped clean, air dried and returned to the shelves. Katy Chou (l) and Sasha Grimman, inventory project contractors, are shown drying wet videotape in the NLM stacks. A small number of printed video guides were too wet for air drying and had to be frozen. NLM keeps freezers on hand for just such emergencies. The guides will be freeze-dried at a later date.
catalogued, tracked and ground into sawdust, powders and gums. These extracts are tested, purified, screened and selected for preclinical evaluation. “Compounds from these extracts which show promise,” Newman says, “will progress toward animal trials.”

It’s a team effort—or, more accurately, teams of teams—and is only the start of a process involving complex negotiations, permits and treaties. Expert botanists and divers are retained to search the hills of Madagascar, the sea trenches of the South Pacific and the desert flats of South Africa. Newman himself travels internationally to manage, liaise and teach.

“We scout plants, microbes and fin-less marine animals in deep and shallow seas,” he explains. Studding the map in his office are sites in Asia, Africa and the Americas, including the arid lands of the southwestern U.S. “We have even had collections in Antarctica,” he says.

The results are impressive: “We have collected 60,000 plant samples and around 15,000 marine samples, including 3,000 algae and microbes,” Newman reports. To put these numbers in context, he reckons that there are around 350,000 plants worldwide, “and at least a million fungi described.” As for bacteria, “We have no idea how many [there are].”

Not a Jigsaw Puzzle

Why go so far afield? Why not just make up drugs from scratch? Newman explains: “Chemists started making libraries of hundreds of thousands to millions of compounds. But these were simple compounds. Mother Nature doesn’t make simple compounds. Mother Nature makes compounds that fit into particular places.”

Moreover, “no chemist in his or her right mind would make up [these compounds] because they don’t know what to make—it’s not a jigsaw puzzle. The intellectual input Mother Nature has is astonishing.”

He tells the story of penicillin, which started as a blue-green mold and a lowly contaminant—an accidental “visitor”—on a hospital lab’s plate culture. Even now, Newman says, when there are over 40,000 variations on the penicillin molecule—almost all made in labs—only 40 have been or still are in use. Chemically tweaked versions of penicillin have been used in the past few decades to make new antibiotics, even an anticholesterol drug.

Natural products make sense, Newman argues, because they work.

The Nautilus in the Freezer

All this borrowing from nature takes time and space, enough to house three-quarters of a million vials, bottles and bags of raw material. “Unfortunately we haven’t gotten Mother Nature to barcode yet,” Newman jokes. “Where it comes from, who collected it and any results—we can see all that by just hitting a button and scanning the barcode.”

A warehouse containing large freezers at minus-20 degrees Celsius stores the treasure trove. Here’s a deep water starfish from Palau. A sea fan. “Shepherdia” that looks like a charming arrangement of twigs. And a rarity—“We had to get special permission for this,” says Newman—a chambered nautilus.

These beauties prompt the inevitable question: What of the risk that people will enter an “exotic” site, steal local knowledge, patent it and not give anything back? “We never wish to be accused of biopiracy,” Newman says. It’s
his responsibility, together with the NCI Technology Transfer Center, to work out collection agreements with host countries: “We are extremely careful about what we collect, who collects for us and under what conditions.”

Tom McCloud, manager of the natural products support group, oversees its laboratory. It is a formidable place that does massive extraction and initial analysis of screening “hits” to find leads to potential drugs. Some of the compounds that his lab has worked on in the past have shown “interesting new biological activities” as anti-HIV and anti-tumor leads.

Other materials from his group include the fungal metabolite wortmannin (a modification of which is in clinical trials for cancer), together with a significant number of other natural products from many sources, now acting as “templates on which to build novel structures” by other chemical groups.

“In my opinion,” says McCloud, “the most important aspect of the DTP Natural Products Repository is that it is available not only for NCI-Frederick, or other NIH researchers’ use, but [also for] research organizations across the country and around the world. We have over 200,000 extracts available for high-throughput screening in both 96-well and 384-well formats, perhaps the largest and most diverse screening library of its kind anywhere.”

McCloud’s lab produces 3,000 extracts a year. How long it takes to separate and identify “actives,” he says, “depends on the number of possible ‘hits’ in a sample,” not to mention funding. As things stand now, “a good chemist with a good tech can separate 10 active extracts in a day in the initial stage of the analyses. And then the time required depends upon the complexity of the compounds and the turn-around time of the biological assays involved.”

While his group does all the extraction and microtiter-plate preparation, “we are not the only ones,” he says, “to do isolation and structure-elucidation work.” This effort is shared by Dr. Jim McMahon’s group in NCI’s Molecular Targets Development Program.

Compounds that pass muster may end as candidates for phase I clinical trials, which, in the life story of a drug, is a turning point. Back on the main campus is an example.

**Biography of a Drug: the Next Chapter**

The plant called *Euphorbia resinifera* is the source of a new drug called resiniferatoxin, or RTX. Dr. Mike Iadarola, chief of NIDCR’s neurobiology and pain therapeutics section, is leading an effort to bring RTX into phase I clinical trials. These studies, designed to prove safety and tolerability, are the first stage of testing in human subjects. In the life story of any drug, phase I is crucial.

“We performed animal studies with good results,” says Iadarola. “We may be able to start clinical trials [very soon]. Here’s a plant providing a solution to something that’s really difficult”—that is, the problem of intractable pain, which RTX can alleviate, he says, with only a single injection. It works by killing a sub-population of pain-responsive neurons, an effect noted in cell culture and *in vivo* using dogs with naturally occurring bone cancer.

RTX is non-opioid—it doesn’t act like morphine, with its attendant risks and side effects—and it is non-addictive. “It binds to the nerve and turns it off chemically,” Iadarola says.

In collaboration with NIDCR anesthesiologist Dr. Andrew Mannes, Iadarola will soon be working with cancer patients in the Clinical Center. And although Iadarola and Newman are in different institutes, on different campuses, they seem to be on the same wavelength—both want to ameliorate cancer and both acknowledge that Mother Nature has a brilliant chemistry set.

That set includes the Euphorbia, the genus name of a rather large group of plants with about 1,600 members—perhaps the most familiar being *Euphorbia pulcherrima*, the poinsettia.

*Euphorbia resinifera*, a type of spurge that grows wild in the Atlas mountains of Morocco, looks to the untrained eye like a cactus that gets bulldozed to build a mall in Arizona. Yet its milky white, latex-like sap, which can be harvested without harming the plant, may prove enormously valuable in relieving suffering.

And although Euphorbia has been known for its medicinal properties for thousands of years, it could, like so many other invaluable species, become endangered only too quickly. In this light, something Newman stressed rings true: Protecting endangered species is closely related to the NPB mission of finding new plant compounds and new drugs.

“This is why we have to stop clear-cutting [forests],” Newman said. “We have no idea what we are losing.”

Top: Newman displays chambered nautilus.
Bottom: Dr. Mike Iadarola, chief of NIDCR’s neurobiology and pain therapeutics section

PHOTOS: MIKE SPENCER
NIH, said Kathryn Lipson, visiting from the University of Massachusetts Medical School. She was one of 244 students who presented posters at the festival.

Students were also able to attend several concurrent scientific sessions on topics ranging from genetics to cancer to cell-matrix interactions.

One of the most popular events proved to be the former trainee panel, featuring six postdoc alums discussing their NIH training experience. The panelists, who now work in a variety of settings, provided insightful overviews of their time here.

“When I was looking for somewhere to go [for postdoc training], I didn’t yet have a clear idea of what I wanted to do,” said Dr. Kathleen Dohoney, who now works for Novartis Institutes for Biomedical Research. “Having so many opportunities here helped me make decisions about where I wanted to go with my career.”

Audience members posed pointed questions to the panelists on everything from the differences between training at NIH and at a university to what kind of conflicts they had here.

Jennifer Sims, from the University of Southern California, found the panel informative. “It was nice to hear about different career opportunities in very realistic terms,” she said.

Lipson agreed, saying the discussion provided practical suggestions for how to go about choosing where to receive postdoc training. “Not everyone will end up here,” she said, “but we’re all going to do a postdoc, so this has all been really useful.” — Sarah Schmelling

Clockwise from top left: Graduate student Laura Barbosky of Duke University happily presents her poster. Dr. Kathleen Dohoney (r) discusses her NIH experience on the alumni panel. Panelist Dr. Nora Gardner takes questions from the audience. As the panel looks on, Dr. Arti Patel Varanasi (l) relays what she learned in her time at NIH.

PHOTOS: MIKE SPENCER
NCI Division Marks 10th Anniversary

The National Cancer Institute is celebrating the research, activities and partnerships of its Division of Cancer Control and Population Sciences (DCCPS) upon the 10-year anniversary of its founding.

“Since its creation in 1997, DCCPS has led NCI’s research to understand the causes and distribution of cancer in populations, to support the development and delivery of effective interventions and to monitor and explain cancer trends in all segments of the population,” said NCI director Dr. John Niederhuber. “Through the highest-quality genetic, epidemiological, behavioral, social, applied and surveillance cancer studies, DCCPS generates new knowledge and helps ensure that the products of cancer control research are effectively applied in all segments of the population.”

DCCPS became a new division at NCI based on recommendations by a special cancer control review group that defined cancer control science as the “conduct of basic and applied research in the behavioral, social and population sciences to create or enhance interventions that, independently or in combination with biomedical approaches, reduce cancer risk, incidence, morbidity and mortality and improve quality of life.”

Dr. Robert Croyle, who currently directs DCCPS, noted the extramural division’s unique role in reducing the burden of cancer in America. “DCCPS has the lead responsibility at NCI for supporting research in surveillance, epidemiology, health services, behavioral science and cancer survivorship,” he explained. “The division also plays a central role within the federal government as a source of expertise and evidence on issues such as the quality of cancer care, the economic burden of cancer, geographic information systems, statistical methods, communication science, tobacco control and the translation of research into practice.”

During the past decade, DCCPS has funded a large and expanding portfolio of grants and contracts. It currently includes over 900 grants valued at almost $400 million. Highlights include:

• Expansion of the Surveillance, Epidemiology, and End Results (SEER) Program, the authoritative source of information on cancer incidence and survival in the United States. Overall, SEER coverage increased from 14 percent to 26 percent of the U.S. population.

• Launch of the Cancer Care Outcomes Research and Surveillance Consortium in fiscal year 2001 to improve the methods and empirical base for quality of care assessment.

• Funding the Long-Term Cancer Survivors Research Initiative focused on questions related to the physiological and psychosocial experiences of cancer survivors 5 or more years post-diagnosis, and interventions to promote positive outcomes.

• Supporting approximately 30 consortia through the division’s Epidemiology and Genetics Research Program. These consortia—which focus on numerous types of cancer and include cohort, case-control and familial studies—conduct the types of large-scale epidemiologic studies needed to address complex questions about the etiology of cancer.

DCCPS relies not only on the expertise of its own scientific staff, but also works closely with other NIH institutes, HHS agencies and nongovernmental organizations. For example, DCCPS, NIDA, NIAAA and the Robert Wood Johnson Foundation jointly fund the Transdisciplinary Tobacco Use Research Centers.

“We look forward to making even greater strides in the coming decade,” said Croyle. “To accomplish this, we will continue to evaluate what has been learned, identify new priorities and strategies and effectively apply new technologies and research discoveries to reduce the cancer burden.”

Top: Dr. Robert T. Croyle, current DCCPS director
Bottom: Dr. Barbara Rimer, first DCCPS director
Del. Christensen Visits NCMHD Council Session

Delegate to Congress Donna M. Christensen (D-VI), who is chair of the health brain trust of the Congressional Black Caucus, told the 16th meeting of the National Advisory Council on Minority Health and Health Disparities that “the caucus and Congress were impressed with the strides NCMHD has made in trying to eliminate health disparities in the U.S. and addressing the disproportionate health burdens suffered by underserved Americans.” Christensen said those accomplishments have occurred under difficult circumstances: “Political and budgetary impediments have made the fight to eliminate health disparities more difficult.”

Council members were heartened by her support and inspired by reports from NCMHD grantees on the front lines in the struggle to eliminate health disparities. As has become common during meetings of the council, center director Dr. John Ruffin asked several researchers to give members new insight into strategies to improve the health of underserved populations.

For instance, Dr. Sonja Harris-Haywood, assistant professor of family medicine at Case Western Reserve University, is taking a hard look at cultural competency. “While this concept is widely accepted as a mechanism for improving outcomes for culturally diverse populations,” she said, “how we define it, measure its presence and test its association with health outcomes in primary care settings is still uncertain.”

Haywood, who is a Loan Repayment Program participant, said she was driven to study medicine and health disparities by the experience of one of her aunts. Growing up in rural South Carolina, Haywood’s Aunt Lula died at home of a ruptured appendix because she was denied care at a segregated hospital. From that point on, Haywood said, her family never trusted doctors. And because of that mistrust, they eschewed treatment for their diabetes and died prematurely because of it. Haywood has dedicated her practice to understanding and alleviating that mistrust in other families.—George A. Strait, Jr.

New Appointments at NCMHD

An award-winning epidemiologist and an advisor to four U.S. Presidents have recently been named to lead NCMHD offices. Dr. Francisco Sy (I), a longtime senior health scientist at the Centers for Disease Control and Prevention and team leader in the HIV/AIDS Prevention Branch, is the new director of extramural activities and scientific programs. Dr. Ileana Herrell, a consultant to the WHO and ILO in Geneva and member of several White House task forces on health and health policy, is new director of scientific strategic planning and policy analysis. Calling them “unique public servants,” NCMHD director Dr. John Ruffin said Sy and Herrell bring the kind of scientific rigor and public health fervor needed to lead the center’s efforts to eliminate health disparities in this country.

Feedback

We don’t have all the answers, but we may know who does. Curious about an NIH matter? Click on the Feedback icon at www.nih.gov/nihrecord/index.htm and we’ll try to track down the info.

Feedback: Why are only two guards inspecting cars at the Natcher vehicle inspection area this week (Oct. 15), instead of the usual four? It now takes twice as long to get through.

Response from ORS: Prior to the guard reductions, there were three, not four, guards assigned to the MLP-7 (Natcher) vehicle inspection. Due to the FY 2008 budget reductions, we were forced to reduce the staffing at that location by one guard. There are now two guards stationed during operating hours at that inspection station. We apologize to our customers if the reductions increase wait-times but it was necessary to meet the decrease in funding for the guard contract.

Feedback: What is the status of the Valve Vault 22 Cold Water Pipe Installation project at the east side of Bldg. 12? The project placard states that construction would last 3 months, ending in August 2006. This is now October 2007! Why is there such a long delay? If the project cannot be completed in a timely fashion, they should close up the huge hole and re-landscape as there has been considerable erosion and run-off caused by the continued lack of plant material on the construction site.

Response from the Division of Property Management, ORF: The project is currently tied up in contracting issues, including securing additional funding to finish the project. The process has gone through several bidding cycles in an attempt to receive a more competitive price to finish the work. The project officer has a meeting next week (Oct. 22) with the bidders to clarify their bids. The project officer hopes to re-start the project before the end of the year.

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An award-winning epidemiologist and an advisor to four U.S. Presidents have recently been named to lead NCMHD offices. Dr. Francisco Sy (I), a longtime senior health scientist at the Centers for Disease Control and Prevention and team leader in the HIV/AIDS Prevention Branch, is the new director of extramural activities and scientific programs. Dr. Ileana Herrell, a consultant to the WHO and ILO in Geneva and member of several White House task forces on health and health policy, is new director of scientific strategic planning and policy analysis. Calling them “unique public servants,” NCMHD director Dr. John Ruffin said Sy and Herrell bring the kind of scientific rigor and public health fervor needed to lead the center’s efforts to eliminate health disparities in this country.
NIH Gains Access to Drug Discovery Resource

NCI and NHGRI recently announced a new project that will provide NIH access to the world’s supply of synthetic chemistry available for drug discovery. Once fully formed, the project will provide a strategy for all NIH scientists to circulate requests for specific chemical samples among thousands, if not tens of thousands, of synthetic chemists at suppliers registered in the system.

Sample quantities will range from milligram up to kilogram. Suppliers will be given tools that allow them to review requests and make proposals to NIH scientists for the synthesis of substances. It is expected that using the new strategy will allow NIH to acquire chemical samples at less than 10 percent of the internal cost of synthesis while offering access to worldwide chemical expertise and diversity.

Medicinal chemists at NCI and NHGRI are currently synthesizing new compounds that may lead to new treatments for disease. Creation of new compounds is slow and expensive. To accelerate the process, NCI’s computer-aided drug design group, led by Dr. Marc Nicklaus in the Laboratory of Medicinal Chemistry at NCI-Frederick, formed an agreement with ChemNavigator.com, Inc., for license to use the iResearch System as a strategy to access worldwide chemistry sources.

ChemNavigator’s iResearch Library (iRL) will provide NIH with a comprehensive source of information on available chemistry for pharmaceutical research. The iRL currently includes over 20 million chemical structures that represent approximately 40 million chemical samples and synthetic building blocks used in early drug discovery. Combined with ChemNavigator’s Chemistry Procurement Service, iRL provides NIH scientists a comprehensive strategy for identifying and procuring available chemical substances. However, ChemNavigator believes iRL covers only a small fraction of the potential chemical substances that could be secured from nearly a thousand commercial, academic and government supplier sources around the world.

Once implemented, the new system will become an archive of commercially accessible custom chemistry products for pharmaceutical research. It is expected that the database will grow to more than 250 million substances in the coming 2 years.

Computer Training Fall Term Now in Session

The CIT Training Program’s fall term of classes is open for enrollment. Classes are offered free for NIH staff. You can obtain full course information, register for classes, join the CIT training mailing list and check out your transcript or current application status at http://training.cit.nih.gov.

CIT’s main campus classroom has added 15 new MacBook Pros, which will run Windows, OS X and Linux; both PC and Mac users can participate in a wide variety of courses and seminars. The facility is also changing from a wireless environment to a wired one, which will increase network speed for scientific classes that require higher bandwidth.

Scientific seminars make up most of CIT’s courses. It offers sessions dealing with Microarray Data, AFNI, MIPAV, the Biowulf Cluster, NCBI Bioinformatics Quick Start, and more. After a long hiatus, this term marks the return of BRB-ArrayTools Data Analysis Workshop.

Statisticians around NIH collect, analyze, interpret or explain and present data. Courses in SPSS (Basics, ANOVA, and Regression), Introduction to Statistical Issues and Procedures Using SUDAAN, and SAS · Statistics I: Introduction to ANOVA, Regression, and Logistic Regression are available.

NIH has a diverse user community, so offerings range from Basic PC Skills for NIH and Intermediate Web-Searching Techniques to Microsoft Visio Professional 2003 Introduction and iSDP Overview. Returning favorites are also available including Excel, Windows XP Tips and Tricks, BlackBerry Tips and Tricks, and Identity Theft: What You Need to Know.

If you have questions about the program, call (301) 594-6248 (voice), (301) 496-8296 (TTY), or email CITTraining@mail.nih.gov.

Alumni Association Ends Successful Run After 18 Years

At its final meeting on Oct. 6, the NIH Alumni Association celebrated a successful 18-year run by reflecting on a number of accomplishments, including continuous publication of a newsletter, NIHAA Update.

Right:
Association President Charles “Chick” Leasure, Jr., congratulates Update editor Harriet Greenwald, who oversaw printing of 40 issues and served as the association’s executive director for all 18 years.

Below:
The association’s last gathering included (from l) current president Leasure and past presidents Cal Baldwin, Dr. Joe Held (who died 3 weeks later, on Oct. 29), Paul Van Nevel, Dr. William Gay and Dr. William Jordan.
NIH Welcomes ‘Emerging Leaders’

NIH recently welcomed five interns who are participating in the HHS Emerging Leaders Program (ELP). They have diverse professional and educational backgrounds, some with multiple advanced degrees in fields such as social work, public health, biological sciences and business administration. They have worked in various capacities in the areas of child welfare, veterinary medicine, cell physiology, health literacy and bone marrow donations. They currently work in offices at NCI, NIDDK, NIAAA and Office of the NIH Director.

The ELP class of 2009 had to compete with some 2,500 highly qualified candidates from all over the country for a few spots in this 2-year leadership development program. Only the top 2 percent of applicants were hired.

The program requires interns to spend 12 months conducting rotational assignments throughout various HHS operating divisions. The interns spend the first 6 months in their NIH home offices before embarking on successive 3-month rotations of their choice throughout HHS. The interns then return to their home offices at NIH for the last 6 months of the program.

In addition to regular work assignments, the interns are required to participate in three formal HHS leadership training sessions per year, which are modeled after HHS competency standards and the Senior Executive Service Candidate Development Program. They must also complete a 6-month group project.

There are currently 21 ELP alumni at NIH. For more information about the program, contact James Peterson at the NIH Training Center, (301) 451-7302.

Three NIGMS Grantees Receive 2007 Gairdner Awards

Three long-time NIGMS grantees were among five recipients of the 2007 Gairdner Foundation International Award. “The 2007 awards reflect the importance of basic discoveries that lead to a better understanding of human disease and the development of treatments and cures to alleviate them,” said Gairdner Foundation president Dr. John Dirks.

Dr. C. David Allis, head of the Laboratory of Chromatin Biology and Epigenetics at Rockefeller University, was honored for his research on chromatin structure and the role of histone modifications in regulating gene expression and maintaining genome stability.

Dr. Harry F. Noller, director of the Center for Molecular Biology of RNA at the University of California, Santa Cruz, and Dr. Thomas A. Steitz, Sterling professor of molecular biophysics and biochemistry at Yale University, were recognized for their separate studies on the structure and function of the ribosome.

In addition, NCI grantee Dr. Dennis J. Slamon of the University of California, Los Angeles School of Medicine was honored for his research on the breast cancer drug Herceptin.

The foundation established the awards in 1957 to recognize the achievements of medical researchers whose work contributes significantly to improving the quality of life. Since its inception, the prize has honored 283 scientists worldwide, 68 of whom have gone on to win Nobel Prizes. Awardees received $30,000 in Canadian funds at an Oct. 25 ceremony in Toronto.
NIGMS Retiree Van Lenten Mourned

Dr. Lee Van Lenten, a former program director and branch chief in the NIGMS Division of Pharmacology, Physiology, and Biological Chemistry, died on Sept. 11 after a brief illness.

He retired in 1995 after 24 years with the Public Health Service, 19 of them with NIGMS. At the time of his retirement, Van Lenten administered research grants in the areas of physiology and trauma and burn injury. He also managed the NIGMS Medical Scientist Training Program, whose graduates receive the combined M.D.-Ph.D. degree.

During his career with PHS, Van Lenten was awarded two Commendation Medals and an Outstanding Service Medal. He was also the recipient of a Golden Apple Award from Georgetown University Medical Center students for teaching biochemistry. A native of New Jersey, he received his A.B. from Colgate University and his M.D. from Yale University School of Medicine.

During retirement, Van Lenten enjoyed gardening, traveling to Europe and helping to maintain the Rockville United Church building.

He is survived by his wife, Beth; a daughter, Deborah; a son, Thomas; and two granddaughters.

Memorial gifts may be mailed to Community Ministries of Rockville, 114 West Montgomery Ave., Rockville, MD 20850 or the Children’s Inn at NIH, 7 West Drive, Bethesda, MD 20814-1509.

NIH Welcomes New Interns

Eleven new Management Interns (MIs) and Presidential Management Fellows (PMFs) recently began 2-year career development assignments at NIH.

The NIH Management Intern Program, established 50 years ago, has graduated over 400 interns and provides a variety of experiences in administrative career fields for highly motivated employees. Through a series of rotation assignments, training, mentoring and career-planning, interns gain hands-on experience in a variety of fields. Joining the program in 2007 are: Aaron Bell, Fettina Bryant, Alan Jackson, Jane Knisely, Virginia Hill, Brian Haugen, Aaron Bell, Andrea Reuss, Molly Puente and Jessica Rodriguez.

Many MI and PMF graduates have gone on to become NIH administrative managers. Janet Dudrick, a 2001 PMF graduate who is now assistant director for management in the Office of Management, says the intern program adds value to NIH: "It is a win-win for all. As an intern with the ability to rotate around and work in different job environments, I had the opportunity to work on projects I never would have had an opportunity to touch and further broadened my skill set."

Dudrick now enjoys having interns rotate through her office. "They bring energy and a fresh perspective," she said, "often creating a synergy that helps push a project forward."

For more information on the intern programs, visit http://internships.info.nih.gov/.

Szabo Receives Biophysical Society Award

Dr. Attila Szabo, chief of the theoretical biophysical chemistry section in the NIDDK Laboratory of Chemical Physics, was one of 14 recipients of the 2008 Biophysical Society awards. He was honored for developing novel theoretical analyses for a wide variety of experiments and bringing leadership to the service of biological physics. Szabo and the other recipients will receive their awards at the joint Biophysical Society annual meeting and IUPAB International Biophysics Congress awards ceremony next February at the Convention Center in Long Beach, Calif.
digest

Many High School Seniors Driving Under the Influence

According to a new study funded by NIDA, nearly a third of high school seniors say they have recently driven while “under the influence,” or they have been in a car with an impaired driver. The findings, published in the *Journal of Studies on Alcohol and Drugs*, are based on data obtained from the Monitoring the Future study that has surveyed high school seniors annually since 1975. The analysis showed that in 2006, 30 percent of seniors reported driving after drinking heavily or using drugs, or riding in a car whose driver had been doing so, at least once within the prior 2 weeks. Study authors stressed that driving under the influence is not an alcohol-only problem and that in 2006, 13 percent of seniors said they drove after using marijuana. Results also showed that the number of teens putting themselves at risk has changed little over the last 6 years. Researchers said all of this news is a wake-up call for the public and that educational efforts need to focus on the dangers of both drinking and drugged driving.

Determining Links to Alzheimer’s

Using a publicly shared genome data set, researchers have been able to strongly support findings that variation in one gene sequence may be a risk factor for late-onset Alzheimer’s disease. Until recently, only one of the approximately 30,000 genes in the human genome had been linked to risk of late onset of the disease; now, it appears that variation in sequence of the SORL1 gene may be a second risk-factor gene. The findings—published in *NeuroReport*, from a study funded in part by NIA—are particularly remarkable because this gene was not a focus of the original study that generated the data used to test the researchers’ hypothesis. They said identifying the genes involved in Alzheimer’s may ultimately help determine who may be at greater risk for the disease and enable researchers to zero in on pathways to develop new treatments.

Assessing the Reach of Dementia

In related news, a recent analysis suggests that one in seven Americans age 71 or older—or about 3.4 million people—have dementia and 2.4 million of them have Alzheimer’s disease. Published online in *Neuroepidemiology*, the NIA-sponsored study is the latest in a series of analyses attempting to assess the prevalence of dementia. It is also the first study to estimate rates of dementia and Alzheimer’s using a nationally representative sample of adults from across the United States. Researchers said these findings highlight the nationwide reach of dementia—for those with the disease, as well as for their families and communities—and warned that as the population ages during the next few decades, the prevalence of Alzheimer’s will increase greatly unless effective interventions are discovered and implemented. The analysis was conducted as part of a sub-study of the Health and Retirement Study, the leading resource for data on the combined health and economic circumstances of Americans over age 50.

Gene Expression and Acetaminophen

Overdose of acetaminophen, the active ingredient in many over-the-counter pain relievers, is the leading cause of liver failure in the U.S. and is often difficult to diagnose. Now, researchers in an NIEHS study report they could detect toxic levels of acetaminophen in laboratory animals by analyzing gene expression in the blood. This research, published online in the *Proceedings of the National Academy of Sciences*, could be a first step in developing accurate new tools to detect acetaminophen overdose in humans, researchers said. It shows gene expression data from blood cells can provide valuable information about acetaminophen levels well before liver damage can be detected by other methods, including serum markers and liver biopsies. — compiled by Sarah Schmelling
The phone numbers for more information about the studies below are 1-866-444-2214 (TTY 1-866-411-1010) unless otherwise noted.

**NIH Pediatric Clinic, Allergy and Asthma Care**
This is an allergy and asthma study for children ages 3 months to 19 years.

**Have Enlarged Gums?**
Do you have enlarged gums and are you taking dilantin, cyclosporine or calcium channel-blockers? Take part in an NIH study.

**HIV+ Volunteers Needed**
HIV+ volunteers off anti-HIV medications, CD4+ count 300 or greater, needed for research study at NIH. Compensation is provided.

**Adults with Neurofibromatosis**
Adults with neurofibromatosis type 1 are asked to consider participating in NIH studies. All study-related tests are provided at no cost.

**Do You Have Ankylosing Spondylitis?**
Consider volunteering for an NIH research study. Compensation is provided.

**Have Trouble Swallowing?**
Are you 20-90 years old and have problems swallowing? Swallowing studies are being conducted at NIH. Transportation is available.

**NIH Turner Syndrome Study**
For girls and women with Turner syndrome—comprehensive evaluation (including cardiac, ovarian function) is offered at no cost to participants.

**Fibroid Study Seeks Women**
Women ages 25-50 suffering with fibroids are asked to consider participating in an NIH study. Compensation is provided. Refer to study 06-CH-0090.

**Neck Pain Study Needs Volunteers**
The Clinical Center’s rehabilitation medicine department is seeking individuals with neck pain and healthy volunteers between the ages of 18-65 to participate in a natural history study of neck pain (02-CC-0245). Participation involves 4 monthly visits (about 1 hour each) for a comprehensive cervical musculoskeletal examination. No compensation is provided. Contact neckpainstudy@gmail.com or (301) 451-7514.

**Panic Disorder Treatment Study**
The anxiety disorders research lab at American University seeks individuals who experience panic attacks to participate in a 7-week psychotherapy treatment study. Participants must be 18 or older and have experienced panic symptoms for more than 1 month. The initial assessment to determine qualification may take 1-3 hours. Qualified volunteers may be eligible for compensation. For more information call (202) 885-1729.

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**NLM Touring Exhibit Celebrates Women Physicians**
The Frieda O. Weise Gallery at the University of Maryland, Baltimore County was recently the site of the opening reception of the national interactive exhibit, “Changing the Face of Medicine: Celebrating America’s Women Physicians,” the traveling version of the 2003-2005 exhibition of the same name that had its beginnings at the National Library of Medicine. UMBC was one of 60 sites across the nation chosen to host it during its 2005-2010 tour. Four of the physicians featured in the exhibition attended the reception. They are (from l) Dr. Marie Amos Dobyns, an Eastern Cherokee American Indian who fully integrates her Indian heritage in her medical practice; Dr. Esther Sternberg of NIMH, who is internationally recognized for her groundbreaking work on the interaction between the central nervous system and the immune system; Dr. Vivian Pinn, the only woman and the only African-American graduate in her class at the University of Virginia School of Medicine and the first (and current) full-time director of NIH’s Office of Research on Women’s Health; and Dr. Pamela Peeke, assistant professor at the University of Maryland School of Medicine in Baltimore, known nationally for her work in nutrition science. Rounding out the group is NLM Deputy Director Betsy Humphreys (far r). The traveling version of “Changing the Face” has been made possible by the American Library Association, the American Medical Women’s Association, NLM and ORWH.

**Pacak Receives Heimann Lecture Award**
Dr. Karel Pacak has received the 2007 Peter Heimann Lecture Award from the International Association of Endocrine Surgeons for his work related to pheochromocytoma. He received the honor recently in Montreal during International Surgical Week 2007. Pacak, who is chief of the section on medical neuroendocrinology, NICHD, spoke on “PET Technology in Endocrine Oncology.” He is also adjunct professor of medicine at Georgetown University and at Charles University, Prague, Czech Republic. His work focuses on diagnosis, pathophysiology and molecular biology of pheochromocytoma. Together with other colleagues from NIH, he introduced the use of plasma metanephrines and 18-F-fluorodopamine positron emission tomography in biochemical diagnosis and localization of pheochromocytoma. In 2005, Pacak established the first international symposium on pheochromocytoma and served as its first president.
Spirits More Generous Than Ghoulish at CFC Halloween Event

On Oct. 31, the annual Combined Federal Campaign Halloween party and charity fair sponsored by the NIH Recreation and Welfare Association drew NIH’ers—many in costume—to the Bldg. 31A patio.

Besides the many witches, mad scientists, superheroes and film stars were dozens of representatives from some of the 3,500 charitable organizations participating in the 2007 CFC.

Prizes were awarded in four categories: Most Like a Movie Star (in keeping with this year’s CFC theme, “Have a Heart/Be a Star”), won by OD’s Laura Toomey, who dressed as Marilyn Monroe; Most Original, won by ORS’s Mandy Slutzker, whose garb proclaimed “Bird Flu Is Not for Birds Anymore”; Most Creative, won by Celeste Gamble of ORS, who dressed as Lottery Queen; and Scariest Costume, won by OD’s Shirley Flottum, who was a mad scientist. Each winner got four movie tickets and a $15 gift certificate to R&W.

Attendees enjoyed lunch provided by Hard Times Café and free Ben & Jerry’s ice cream donated by the NIH Federal Credit Union.

Counter-clockwise from top right:
Waiting in line for their lunch tickets were (from l) Josh Duberman of NLM and Verma Walker and Brigit Sullivan, both of ORS.

Biker Josh Rose of ORS mugs for the camera with mad scientist Shirley Flottum of OD, who won Scariest Costume. NCI’s Wallace Rumbarger is at rear.

Striking a menacing pose is the winner of Most Original Costume, ORS’s Mandy Slutzker, whose garb proclaimed “Bird Flu Is Not for Birds Anymore.”

Stefanie Coburn of ORS said she was a “Virgin Runaway Bride.”

OD offices yielded movie stars (from l) Spiderman (Jonathan Lappin), Marilyn Monroe (Laura Toomey, who won Most Like a Movie Star) and the Hulk (Sean Sommers).

Right:
Celeste Gamble (l) of ORS was dressed as Lottery Queen and won Most Creative Costume.

Far right:
Many witches flew in for the occasion, including this not-so-wicked-looking one.

PHOTOS: RICH MCMANUS AND JANET STEPHENS