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The Second Best Thing About Payday

nih record

ABOVE • *Did you know that the U.S. and Iran have research collaborations? See p. 7.*

features

departments

The NIH Record is recyclable as office white paper.

New FAES Executive Director Focuses on Building

By Carla Garnett

Nearly 12 months into her new job as executive director of the Foundation for Advanced Education in the Sciences and Christina Farias could sum up her first year here in one word: "building"—as in constructing new digs, forming new partnerships and framing new directions.

For a long while, much of what Farias knew about NIH was hearsay. Her neighbors—both NIH employees—were unofficial ambassadors for the agency. "One is a scientist and one is a lab manager," Farias explained, "and I'd heard from them such glowing talk about the NIH community that I admired NIH from a distance for some time. I've always leaned toward working for non-profits and organizations with missions that involve helping people. So when the FAES job was advertised, it just seemed like a perfect fit."

Before taking her new position, Farias did a fair amount of research on FAES and its history of

SEE **FARIAS**, PAGE 4

FAES Executive Director Christina Farias

Got Ginger?

Dong Speaks on Nutritional Foods, Cancer Prevention

By Belle Waring

Cancer remains one of the leading causes of death in today's world, says Dr. Zigang Dong, director of the Mayo Clinic's Hormel Institute and professor at the University of Minnesota.

He recently visited NIH to give a talk titled "Can We Win the War Against Cancer by Prevention?" This was part of the Stars in Nutrition and Cancer Lecture Series, sponsored by NCI's Division of Cancer Prevention.

Many kinds of cancer trends—including the incidence of lung and stomach cancer—are going down, he said. And yet in the U.S., the total cancer incidence and death rate has dropped only slightly.

SEE **CANCER PREVENTION**, PAGE 6

Researchers Hunt for Causes of Nodding Syndrome

By Kathryn DeMott

Clusters of children living half a world away have the most seasoned global disease experts stumped.

The children have an epileptic encephalopathy called nodding syndrome, a neurological condition for which there is no known cause and that affects thousands in rural African villages, according to Dr. Scott F. Dowell, director of the division of global disease detection and emergency response at the Center for Global Health (CGH), Centers for Disease Control and Prevention.

Dowell and Dr. James Sejvar, a CGH medical officer, shared what is known to date about the mysterious condition at a recent grand rounds session sponsored by the National Institute of Neurological Disorders and Stroke. Dowell reviewed findings from 4 case-control studies involving 486 subjects including 121 age- and village-matched case-control pairs in South

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NIH...Turning Discovery Into Health

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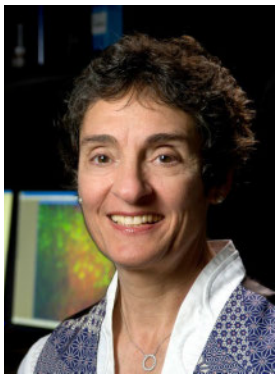
briefs

Wood To Keynote King Observance, Jan. 24

NIH's 2013 Dr. Martin Luther King, Jr., observance will be held on Thursday, Jan. 24, from 11 a.m. to noon in Wilson Hall, Bldg. 1. The national theme for the 2013 King holiday is "Remember! Celebrate! Act! A Day On, Not a Day Off." The MLK day of service is a part of United We Serve, the President's national initiative. It urges Americans from all walks of life to work together to provide solutions to our most pressing national problems. Dr. Lauren Wood, staff clinician in the National Cancer Institute's Vaccine Branch, will be keynote speaker. Her presentation is titled, "Clinical Translation of Therapeutic Cancer Vaccines: From Bench Discoveries to Bedside Realities."

Sign language interpreters will be provided. Individuals with disabilities who require reasonable accommodation to participate should contact Victoria Gross at (301) 451-0746, through the Federal Relay Service (1-800-877-8339) or via email at Victoria.Gross@nih.gov.

Shatz To Give NIH Director's Lecture, Jan. 23



Dr. Carla J. Shatz, professor of biology and neurobiology at Stanford University, will deliver the first of three NIH Director's Lectures as part of the 2012-2013 Wednesday Afternoon Lecture Series. Shatz's lecture, "Circuit Tuning During Developmental Critical Periods: Immune Genes Moonlighting in the Brain," will be held on Wednesday, Jan. 23 at 3 p.m. in Masur Auditorium, Bldg. 10. For more information on Shatz's research visit www.stanford.edu/group/shatzlab/. For lecture information and reasonable accommodation, contact Jacqueline Roberts, (301) 594-6747.

PHOTO: STEVE FISCH

STEP Forum on Vitamin D, Feb. 7

The staff training in extramural programs (STEP) committee will present a Current Controversies in Medicine forum on the topic "Got (Enough) Vitamin D?" on Thursday, Feb. 7, from 9 to 11 a.m. in Lister Hill Auditorium, Bldg. 38A.

Vitamin D is vital for the development and maintenance of healthy bones and skin. New evidence suggests that this natural substance is also involved in immune and muscle functions. Yet abnormal vitamin D levels may play key roles in cancer, infertility and other disorders. What is this essential substance, how is it made in the body and what does it really do for us? What are optimal levels of vitamin D and how are they affected by genetics, environment, age and diet? Join us to learn more about the "sunshine" vitamin's role in human health and disease.

Join the NIH-HHS Mentoring Program

NIH wants you to join the HHS Mentoring Program. Federal employees interested in serving as mentors and mentees across the NIH community are invited to join the NIH January 2013 cohort.

The free program features:

- Peer-to-peer and senior-to-junior mentoring relationships
- Online application and matching system to connect individuals
- Online mentor-mentee orientation
- 1-year mentoring relationship commitment
- Professional development events and activities

For more information, visit http://trainingcenter.nih.gov/HHS_Mentoring.html or email nihhhsmentoringprog@od.NIH.gov.

Have a Family History of Alcohol Addiction?

The National Institute on Alcohol Abuse and Alcoholism is seeking men and women ages 21-30 with a family member (parent or sibling) with a history of alcohol addiction. The study seeks to identify genes that are related to the response to alcohol in humans (study 11-AA-0180). Volunteers should be healthy and drug-free. Qualified participants will be reimbursed for their participation. The study involves a screening visit and two outpatient visits at the Clinical Center. For more details and to participate, call (301) 435-9397 or email AlcPGstudy@mail.nih.gov.

Dr. David G.I. Kingston recently delivered the NCCAM Straus Lecture.

PHOTO: LISA HELFERT

Straus Lecturer Describes Promise in Herbs, Natural Products

By Ellen O'Donnell

Recently, Dr. David G.I. Kingston delivered the 2012 Stephen E. Straus Lecture in the Science of Complementary Health Therapies, "Natural Products: Drugs for All Reasons and All Seasons." NCCAM's lecture series honors its founding director.

Kingston is professor of chemistry and university distinguished professor at Virginia Polytechnic Institute and State University, director of the Virginia Tech Center for Drug Discovery and an NIH grantee. Among his achievements are pioneering research on paclitaxel, an anticancer drug derived originally from the yew tree, and on medicinal plants in tropical rainforests.

There are up to 50,000 traditional plant medicines, said Kingston, and worldwide they have a high rate of use. In the United States, the 2007 National Health Interview Survey found that 17.7 percent of Americans used natural products in the year prior to the survey, making them the most-used complementary health approach.

Natural products and their compounds have an important role in drug discovery, Kingston said, and are well suited by their nature to that enterprise. From 1981 to 2010, 34 percent of approved new drugs were either natural products or modifications of them; in anticancer drugs the figure is 43 percent. Current advanced research techniques "allow us to do things today we couldn't do even 10 years ago," said Kingston.

In the future, natural products could add—alone and in combination—to established treatments; be aimed at new disease targets, such as the modulation of protein interactions; and offer new hope for treatments for various diseases that are scourges of the developing world but receive little attention in conventional pharmaceutical research. A few examples are malaria, diarrhea and leishmaniasis. "We can impact the world," Kingston urged.

Safety must be carefully examined, as natural products can have adverse side effects and can interact with other substances such as drugs. Kingston noted that these interactions need much more research.

For the past 15 years, he has led a large cooperative research program, co-funded by NIH, in Madagascar, an island nation off the coast of Africa that has a rich but threatened ecosystem. In an innovative approach, the international cooperative biodiversity group links three goals: drug discovery from plant and marine sources, conservation of biodiversity and economic development of the local area.

An earlier site was Suriname, in South America. Among the program's effects have been the discovery of new drug leads, creation of new protected areas and several infrastructure improvements.

Congressional Staffers Tour NIAMS Labs

Eight senior-level congressional staffers recently toured laboratories of the National Institute of Arthritis and Musculoskeletal and Skin Diseases. The group represented both Republicans and Democrats from the House and Senate, including members of NIH's authorization and appropriations committees. The visit was organized by the NIAMS Coalition, an independent group of more than 70 professional and voluntary organizations concerned with NIAMS programs, to help build awareness on Capitol Hill about research advances in NIH labs that are leading to significant improvements for patients. NIAMS leaders and scientists (shown above with the Hill staffers) gave overviews of NIH and described breakthroughs in translational research. They emphasized the possibilities for discoveries, the importance of maintaining a pipeline of research scientists and the value of partnerships among government, private industry and professional and patient groups. "This is an exciting place to be," said NIAMS director Dr. Stephen Katz. "There has been a deluge of discoveries and the opportunities for translational research are unprecedented."

PHOTO: BILL BRANSON

FARIAS

CONTINUED FROM PAGE 1

supporting the nation's medical research agency. She arrived with a plan.

"I want FAES to build new relationships, provide new wonderful services, find new ways to be supportive and spur innovation and creativity," said Farias, "and be a place where people can talk about wonderful ideas over cookies."

"I want to help FAES move into the 21st century. I want us to modernize without losing sight of our core mission, which is helping NIH further advance research in human health for the benefit of everyone."—Christina Farias

With a current staff of about 18, FAES recently marked 53 years as the non-profit organization created by NIH scientists to administer what started as a "Graduate Evening Program" of advanced classes to supplement lab training. The program was immediately popular and grew rapidly. FAES's graduate school now offers almost 200 courses every year, ranging from "Immunofluorescence and Confocal Microscopy" to "Argentine Tango: Learn About It and Dance," with nearly every biological science and general subject in between.

"I've been quite amazed at everything we do with so few people," Farias said. "NIH has more of a collegial feel than some higher education places I've been to. I work with such incredible people. It's a joy coming to work every day."

This spring, FAES staff—currently working in several sites on and off the NIH campus—will reunite in the Clinical Center. A newly constructed 20,000-square-foot facility in the heart of Bldg. 10 will contain eight classrooms, a bookstore, coffee bar, grad student lounge and a suite of administrative offices.

Underwritten by FAES, the "$10 million construction project is donated entirely to NIH," Farias noted. Funded by revenue generated from its bookstore and graduate school, and the health insurance program it offers to NIH's visiting international scientists, the foundation is financially self-sustaining.

"I can't wait until we get everyone working under one roof again," said Farias, whose office is in Bldg. 60. "Our new space will allow us to offer webcasting, online as well as traditional courses, distance learning and a lot more. We'll be able to do a wide range of things, from small conveniences—like providing snacks for lectures—to hosting high-profile speakers and instructors from such places as NASA, Johns Hopkins and Georgetown. We're looking to evolve to fit the needs of the community."

Located on two floors under a skylight known for years by CC denizens as "the donut hole," FAES's new home represents a collaboration between the foundation and NIH. FAES will be sharing the space with NIH's Office of Intramural Training and Education, Office of Research Services, Events Management and the Clinical Center during the day, with FAES courses being held primarily in the evening.

The student population and faculty from across campus—OITE's fellows committee, Felcom, in particular—are working closely with Farias and her team, making suggestions on ways to enhance the student experience here. The new classrooms and new bookstore were designed to strengthen the collegial feel of the campus by hosting courses and seminars across disciplines and offering a wide retail selection and gourmet coffee just steps away from Masur Auditorium.

No stranger herself to the campus lifestyle, Farias, a southern California transplant who's lived in the D.C. metropolitan area for about 12 years, has an undergraduate degree in business management from Johns Hopkins University's Carey Business School and a master of science degree in management and internal auditing from the University of Maryland Smith School of Business. She's currently pursuing an M.B.A. at the Smith School.

"My experience focuses primarily on non-profit business functions—the majority in higher education in the areas of finance, business, property and lease agreements, academic programs, student and auxiliary services," she said. "My specialties are operational, financial and human capital management." Her higher education experiences have been with Georgetown University Law Center and the main GU campus, JHU's Montgomery County campus and the University of California, Riverside.

"There was a tiny bit of culture shock when I got here," Farias admitted, describing both the charm and the challenges of working in Bldg. 60, a 90-year-old structure built as a convent. "We just got [wireless capability] not too long ago and that was a huge accomplishment."

But the rich history of NIH and the foundation are a large part of what drew her here and Farias believes there is a lot of benefit in combining old and new.

"I want to help FAES move into the 21st century," she concluded. "I want us to modernize without losing sight of our core mission, which is helping NIH further advance research in human health for the benefit of everyone."

digest

Coordinated Care Can Address Disabled Adults' High Rates of ER Use

Working-age adults with disabilities account for a disproportionately high amount of annual emergency department visitors, an NIH comparison study has found. As emergency department care may not be the best to address nonurgent concerns and is higher in cost, finding a way to decrease these visits is of interest to many stakeholders.

One of the first detailed looks at this population's heightened use of urgent care, the NIH study published online in *Health Services Research* on Dec. 26, 2012, analyzed pooled data from the Medical Expenditure Panel Survey. Researchers found access to regular medical care, health profile complexity and disability status contributed to people with disabilities' use of the emergency department. To address this disparity, the authors recommend enhanced communication between emergency department and primary care physicians and tailored prevention and primary care programs.

"We want to understand what takes people to the emergency department to learn if their care could be better managed in other ways," said Dr. Elizabeth Rasch, chief of the epidemiology and biostatistics section in the Clinical Center's rehabilitation medicine department. "While many of those visits may be necessary, it is likely that some could be avoided through better information-sharing among all of the health care providers who see a particular individual."

The study found that, despite representing 17 percent of the working-age U.S. population, adults with disabilities accounted for 39.2 percent of total emergency room visits. Those with a severely limiting disability visited an urgent care department more often than their peers and were more likely to visit the department more than 4 times per year. Emergency visits were also associated with poor access to primary medical care, which was more prevalent among adults with disabilities.

Benefits of Higher Oxygen, Breathing Device Persist After Infancy

By the time they reached toddlerhood, very preterm infants originally treated with higher oxygen levels continued to show benefits when compared to a group treated with lower oxygen levels, according to a follow-up study by an NIH research network that confirms earlier network findings. Moreover, infants treated with a respiratory therapy commonly prescribed for adults with obstructive sleep apnea fared as well as those who received the traditional therapy for infant respiratory difficulties, the new study found.

"CPAP [continuous positive airway pressure] for infants has been available since the 1970s," said senior author Dr. Rosemary D. Higgins of NICHD; NHLBI also supported the study. "This is the first study to compare surfactant treatment to CPAP in a large group of infants, and these results reassure us that CPAP is as good a choice in the first hour of life as traditional methods for very preterm babies who need help breathing. We've also confirmed that higher oxygen targets improve survival and don't appear to threaten survivors' vision in the longer term."

The findings appeared in the *New England Journal of Medicine*.

By the time they reached toddlerhood, very preterm infants originally treated with higher oxygen levels continued to show benefits when compared to a group treated with lower oxygen levels, according to a study by an NIH research network.

Gene Variation May Shape Bladder Cancer Treatment

Patients who have inherited a specific common genetic variant develop bladder cancer tumors that strongly express a protein known as prostate stem cell antigen (PSCA), which is also expressed in many pancreatic and prostate tumors, according to NIH research.

A therapy targeting the PSCA protein on the tumor cell surface is under evaluation in clinical trials for prostate and pancreatic cancer. The researchers hope that this therapy will be tested in bladder cancer patients with the genetic variant, which could help reduce potentially harmful side-effects, lower costs and improve treatment efficacy.

"We've been pursuing this mechanism for some time now," said NCI's Dr. Ludmila Prokunina-Olsson, senior author of the paper. "It started with our early results from the initial genome-wide association study that revealed a marker in the PSCA gene related to bladder cancer risk. This latest work reveals how a specific letter change in DNA influences protein expression at the cell surface. The big payoff is that a simple genetic test can determine which patients could benefit from anti-PSCA therapy."

The paper appeared Jan. 3 in the *Journal of the National Cancer Institute*.

CANCER PREVENTION

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***Above**:*
"Cancer and prevention are tightly linked," Dong told the audience in Bldg. 10's Lipsett Amphitheater.

PHOTOS: BILL BRANSON

Prevention is critical to lowering the worldwide incidence of cancer, still the number 1 cause of death for Americans under 80.

"Cancer and prevention are tightly linked," Dong told the audience in Lipsett Amphitheater. A leader in research on ultraviolet light-induced skin cancer, he focuses on its molecular mechanisms in mouse models.

"I would like to emphasize that we have a lot of achievement," he said, "but it's not good enough compared to scientists in the cardiovascular disease area. They have a very strong prevention program."

One of Dong's major goals is to identify agents with low toxicity, fewer side effects, usable alone or with traditional chemotherapeutic agents to prevent or treat cancer.

Why the focus on nutritional foods?

The idea of food as medicine, said Dong, is not a new one. Many dietary factors have potent anticancer activities, but they work through mechanisms that are still unknown.

Cancer is complicated, with a multistage process of initiation, promotion and progression. Preventing it is also complicated. For one thing, a study in prevention can be more difficult than a study in disease, where you can more readily see an effect.

And isolating beneficial plant compounds, called phytochemicals, is tricky. It's also hard to study them as a mixture: Do you look at substances A and B—or B and C—or the whole thing together?

So is green tea good for you? Its phytochemicals may be biologically meaningful, but they don't necessarily translate to clinical applications. Yet.

"So please don't think of this as a lecture," said Dong, who completed postdoctoral training at NCI-Frederick. "This is just a progress report by an NIH-trained student."

To appreciate that progress, think of the body as an intricate network of cells in a constant, but stable, state of change.

Then imagine a single cell as a microscopic city-state that produces a lot of industry and commerce within its walls. It also communicates with the domain outside those walls. Its boundaries are dynamic, busy with sending and receiving stations. Some stations are like piers where external molecules from hormones, food or drugs can pull in and dock—blocking other molecules in the process. Or they may be allowed entry into the cell itself.

To do its work, the cell makes its own molecules for signaling, pathway and transduction (the transfer of genetic material). These let the cell read and adapt to events both inside and outside its walls. Such microscopic cellular processes are so complicated that they make our vast human bureaucracies look simple.

And to complete all these tasks, the cell needs work orders. These are found in the genes, which contain DNA, the set of instructions for making proteins (the building blocks of life) as well as RNA (the intermediary). How these instructions develop depends on the specifics and the timing of gene expression.

Expression is a crucial process, because it turns the gene's instructions into something the body can use, like the proteins that operate our cells.

Genes can also contain mutations implicated in cancer.

Working on this intricate microscopic level, Dong investigates the cell's response to tumor promoters. These are like docking stations for proteins that control when genes are expressed.

He also studies protein kinases, enzymes that modify other proteins. Protein kinases have profound effects on a cell, as they regulate the majority of cellular pathways.

By focusing on these specific molecular mechanisms, Dong has discovered that several are critical in cancer development.

His lab has also identified key molecular targets for screening novel natural anticancer drugs with fewer side effects. Many of these com-

"This is my dream," said Dong, "to rewrite the history of nutritional science."

pounds appear to act on tumor-promoter-stimulated pathways.

Various dietary factors—including those isolated from green and black tea, broccoli, red grapes, ginger root and rice—can have effects on key signaling molecules.

"Our lab focused on green tea and ginger," Dong said. "When gingerol was painted on mouse skin it was found to be more powerful than the control with a conventional chemotherapeutic agent." To find the mechanism for how gingerol works, his lab has chosen it for further study.

He has also taken a major step in understanding the mechanisms of anticancer effects of green tea in the mouse model.

Green tea now looks promising, but Dong cautioned that we cannot assume that nutritional compounds are safe. For example, some reports now show that capsaicin, the "hot" ingredient in spicy peppers, may have cancer-causing effects.

More large-scale animal and molecular biology studies are still needed to address the bioavailability, toxicity, molecular targets, pathways and side effects of dietary factors. There are currently two clinical trials in breast cancer prevention at the University of Minnesota.

"This is my dream," said Dong, "to rewrite the history of nutritional science."

U.S.-Iran Scientific Partnerships Hold Promise

Scientific engagement between Iran and the United States is flourishing and includes a number of research partnerships involving NIH.

Several Americans, led by an NIH grantee, traveled to Iran recently for the country's first international and fifth annual HIV/AIDS conference. It was organized by UNAIDS and the Iranian Research Center for HIV/AIDS, part of Tehran University Medical School. Topics ranged from the prevention of mother-to-child transmission, to harm reduction through examination of transmission routes, to strategies to strengthen Iran's overall response to HIV/AIDS.

NIAID grantee Dr. Navid Madani helped organize the event. The Iranian-born Harvard scientist said she received a warm response from the host scientific community. "Iranians place a high value on establishing international scientific collaborations and in building research capacity in their country," she noted.

There are a number of longstanding research collaborations between NIH and NIH-funded researchers and their Iranian counterparts on topics including cancer, heart disease, hepatitis and opiate addiction.

In the case of HIV/AIDS, Iran's approach provides a useful model, Madani suggested. "Iran can be the beacon for all the countries around it." Iranian health officials have taken measures to decrease both the HIV infection rate and the disease's stigma, she said. In addition, they offer free condoms, voluntary testing and include prison inmates in their outreach.

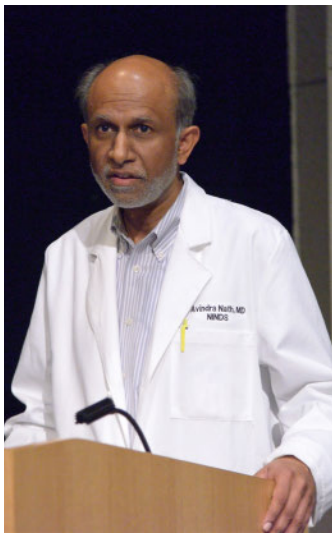
"We can learn so much from Iran and its grassroots model of health houses in each village, not just to benefit our primary health care but also our approach to HIV prevention and care," said Madani.

The country's latest strategic plan to combat HIV/AIDS acknowledged the virus is increasingly spread through sexual contact. With more than 24,000 Iranians testing positive for HIV—the vast majority male—this was a critical breakthrough, Madani said.

"The scientific interactions were quite positive," she observed. "In addition to this stimulating scientific dialogue, we had an absolute goldmine of people understanding each other and a unique cultural and scientific exchange."

Iranian-born Harvard scientist Dr. Navid Madani (l), an NIAID grantee, helped organize Iran's first international HIV/AIDS conference.

PHOTO: TEHRAN UNIVERSITY OF MEDICAL SCIENCES



NODDING SYNDROME

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***Above, from l**:*
Dr. Scott F. Dowell (l) and Dr. James Sejvar, both of the Centers for Disease Control and Prevention, field questions about nodding syndrome at their grand rounds presentations on the mysterious illness that affects children in rural African villages.

Dr. Avindra Nath, NINDS clinical director, said the forthcoming vitamin B6 trial will provide an opportunity to follow patients prospectively and to collect biological samples from well-characterized patients.

PHOTOS: BILL BRANSON

Sudan and 122 pairs in Uganda. Some 10 investigations have been conducted; only the 4 have been case controlled.

Initially described in Tanzania during the 1960s, the syndrome causes children to experience epileptic episodes that involve nodding their heads forward 10 to 15 times a minute in a non-rhythmic fashion for about 5 minutes during which they do not respond to commands, Sejvar explained. EEG findings from his case-control study in Uganda confirmed the presence of atonic seizures.

The nodding episodes are most often triggered by the aroma of food or exposure to cold weather, suggesting that the cause of the episodes may have a reflexive component, Dowell added.

Within a few years, most children with the syndrome progressively worsen. The nodding episodes, which at first occur a few times a week, start happening several times a day and are increasingly followed by general confusion, incontinence and lethargy. Eventually, multiple seizure types develop involving convulsions and staring spells. Mental capacity greatly diminishes and school performance declines. Some families resort to securing the children to trees to keep them from wandering and harming themselves by drowning, falling or fire exposure. Early mortality is common, though it is not clear at this point if the deaths are due to the syndrome's progression or the circumstances that it creates.

Children with the syndrome generally are reported to be healthy until nodding episodes begin. Fully 93 percent of the children evaluated in Uganda were ages 5 to 15 years, Dowell said.

Geographically, the cases are concentrated in rural pockets of South Sudan, Uganda and Tanzania, affecting as many as 40 per thousand children in some villages. Yet these clusters are separated by hundreds of kilometers with no known cases. Urban populations appear unaffected.

Among the speculated causes of nodding syndrome is *Onchocerca volvulus*, an infection spread by blackflies that breed in fast-flowing streams and then inject their larvae into a human host. That same parasite causes onchocerciasis, otherwise known as river blindness, which is endemic in regions where nodding syndrome also is prevalent. In one of the case-control studies in South Sudan, *Onchocerca* infection was more common among the 38 cases compared to controls (76 percent vs. 47 percent).

Genetics also may be a contributing factor; polygamy is practiced in the regions. A genetic mutation that, for example, makes some children less responsive to ivermectin, the treatment commonly used for onchocerciasis, could quickly gain a foothold in populations where polygamy or inbreeding is practiced.

Many of the affected communities were displaced by civil war conflicts in the late 1990s and toxin exposure during that period cannot be ruled out. Consumption of improperly prepared cassava root, a common staple in the region, can lead to cyanide poisioning.

Another hypothesis involves nutritional deficiencies. In at least two of the case-control studies, children with nodding syndrome were more likely than controls to have vitamin B6 (pyridoxine) deficiencies. This is intriguing, Dowell said, because pyridoxine-dependent seizures are known to resolve with vitamin B6 supplementation. However, most of these types of seizures begin before age 3 years, so the relevance of vitamin B6 deficiency in terms of nodding syndrome is still unclear.

As part of a general intervention, many of the children have been taking a multivitamin, but therapeutic levels may be several 100-fold higher. A clinical trial to investigate the effects of therapeutic levels of vitamin B6 among children with the syndrome is set to launch in 2013.

Dr. Avindra Nath, NINDS clinical director, said the vitamin B6 trial is an excellent idea. While it may not lead to a silver-bullet treatment, "it will certainly be an opportunity to follow patients prospectively and collect biological samples from well-characterized patients, all of which will be very useful in studying the disease."

milestones

NIDDK Epidemiologist Eggers Retires

By Anne Wright

It's no surprise that Dr. Paul Eggers has become synonymous with the U.S. Renal Data System (USRDS). The NIDDK epidemiologist has devoted most of his public service career to developing and refining what has become the most well-known and respected kidney disease registry in the world.

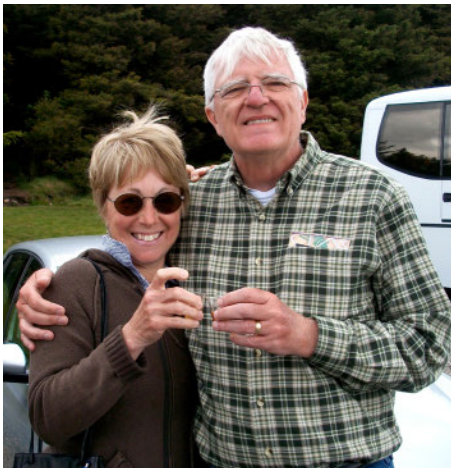
Eggers, who worked at the Health Care Financing Administration (HCFA) for 22 years before joining NIDDK in 2000, will ease into retirement this month. Though he will no longer manage his grants portfolio, he will continue to serve as part-time program director for the USRDS and the Urologic Diseases in America Compendium, the urology equivalent of the USRDS.

"Paul is at the heart of the USRDS and his efforts on behalf of the registry have truly been a labor of love," said NIDDK director Dr. Griffin Rodgers. "We are fortunate that he will continue to lend his knowledge and expertise to the research community after he formally retires."

The USRDS, a joint project of NIDDK and the Centers for Medicare and Medicaid Services (CMS), formerly HCFA, began in 1987. The registry produces an annual data report summarizing the incidence, prevalence, morbidity, mortality and costs of end-stage renal disease (ESRD). CMS and Congress are especially interested in this data because Medicare has been covering people of any age with ESRD since 1972. The registry also provides access to data sets for kidney research scientists.

"Dr. Eggers is a national treasure," said Dr. Robert Star, director of NIDDK's Division of Kidney, Urologic and Hematologic Diseases. "In his 35-plus years of national service, he ensured the integrity of each and every data point in USRDS, supported scientists with innovative analyses and spotted emerging trends. He was completely dedicated to producing the best science that would improve the health of patients with kidney disease."

"A large number of nephrologists use the USRDS to identify helpful and harmful trends in dialysis and transplant populations, which helps physicians deliver better patient care and investigators plan research efforts," said Dr. Paul Kimmel, director of the Acute Kidney Injury Program, Kidney Translational Genetics Program and Kidney HIV Program at NIDDK. "The USRDS also produced data showing disparities across geographic areas, which can be used to establish best practices in caring for patients with ESRD."



Dr. Paul Eggers and his wife Anne toasted to "good times" during a recent trip to Ireland.

As the nation's "premiere expert" of ESRD data, Eggers has served as a global resource for all nephrologists and mentor to hundreds of investigators who use the USRDS as a research tool, according to Dr. Chris Ketchum, NIDDK's deputy director for basic renal physiology and diabetic nephropathy programs. "His paradigm-shifting early studies and speaker presentations have spawned a fertile, large new research field for nephrologists. Over his illustrious career, there is little question that Dr. Eggers' commitment to federal service has made an enormous impact on our understanding of kidney disease and the nation's public health," said Ketchum.

Eggers has been instrumental in showing that acute kidney injury is a key risk factor for chronic kidney disease and that frequent hemodialysis affected intermediate medical outcomes and patient perceptions of quality of life. The author or co-author of nearly 120 journal articles, his earliest papers outlined key outcomes in the ESRD program and documented disparities in hemodialysis survival and access to kidney transplantation.

"Dr. Eggers' early work showed less access to transplantation among minority groups with ESRD—a situation clinicians and policymakers have been struggling to rectify over the past 20 or more years," added Kimmel. "His work on amputation in the ESRD program has been followed by a decrease in the complication rate in diabetic ESRD patients in the U.S."

Eggers' research contributions extend beyond kidney disease as well, according to Marian Gornick, Eggers' former supervisor at HCFA, now retired. One example is his design of a system for coding medical services, known as Berenson-Eggers Type of Service, which HCFA, other federal agencies and private organizations adopted. Another was his co-authorship of a major study of disparities in Medicare services use titled "Effects of Race and Income on Mortality and Use of Services among Medicare Beneficiaries," which was published in the *New England Journal of Medicine* in 1996.

"Dr. Eggers was known for his leadership, encouragement and support of his staff," said Gornick. "He perhaps was the most respected and admired branch chief in the [HCFA] Office of Research."

Though Eggers will not fully relinquish his desk job, he looks forward to spending more time outdoors. "My wife, Anne, and I are really big on national parks and rural adventures," he said. "We are going to try to devote more time to that."

A self-described World War II enthusiast, Eggers also is anticipating having more time to make a dent in his ever-growing reading list. "There's always a new book coming out about World War II," he said. "Over the years, I've compiled dozens of books I want to read."

In addition, he looks forward to donning a brand new role—that of first-time grandfather.

"After 36 years of doing essentially the same thing, it's hard not to define yourself to a great extent by what you do," said Eggers. "I hope part-time work will be a good segue into full-time retirement."

NIGMS's Anderson Finds Balance, Adventure in Retirement

By Alisa Zapp Machalek

One of Dr. Jim Anderson's goals in retirement is to pay more attention to his dog Nicky, who he says "always wakes up happy."

Flow like a river, stay rooted like a mountain. That t'ai chi concept of life balance has long guided NIGMS's Dr. James J. "Jim" Anderson. Now that he's retired, Anderson finds himself flowing into new—and sometimes surprising—opportunities while remaining rooted in his lifelong interests.

Trained as a microbial geneticist, Anderson came to NIGMS in 1990 after working in the biotech industry for 10 years. At NIGMS, he managed an extramural grant portfolio in gene regulation in the Division of Genetics and Developmental Biology. The portfolio included investigations of diverse microbial communities (microbiomes) that are integral to human health; studies of bacterial communication; and research on prions, infectious protein particles that can cause fatal neurological diseases.

During Anderson's 22-year career at NIGMS, he witnessed a growing scientific understanding of how organisms tune their genes to address changes in their environments. On one especially memorable day, he recalls reading a progress report in which Dr. Andrew Fire "almost casually" described his observation that double-stranded RNA can silence genes. Anderson was stunned by the significance of the finding. He immediately called Fire to congratulate him and discuss the work's implications. A scant 9 years later, Fire shared a Nobel Prize for the discovery of RNA interference.

In addition to advising individual grantees, Anderson worked more broadly to shape the direction of research.

"Jim always stood out as a person with creative and forward-looking ideas, which he championed and often brought to fruition," said Dr. Judith Greenberg, acting NIGMS director and long-time director of Anderson's division.

Examples include the creation of the *E. coli* K-12 model organism resource, a comprehensive online repository of information about a bacterium studied by many researchers (including Anderson).

He also developed some of the institute's earliest programs to support systems-level modeling and computational biology. He describes the emergence of these fields as "the reincarnation of physiology, with the added punch of genomics and advanced analytical technologies."

NIGMS-funded researchers and others now routinely use computationally driven approaches to organize and analyze vast amounts of data, generating models with a range of applications, from predicting the effects of medications on cellular systems (and, potentially, on human physiology) to indicating the impact of public health interventions on the spread of infectious diseases.

NIGMS colleagues remember Anderson as the microbiome guru, the resident plant champ (an advocate for research on plant model systems and a connoisseur of home-grown figs and paw paw fruit), a bicycle commuter and the volunteer instructor of t'ai chi classes.

Anderson sees retirement as "a marvelous open road" and looks forward to exploring wherever it leads. He plans to do more cycling, traveling (including visits to his extended and far-flung family), gardening and concert-going with his wife, Janet.

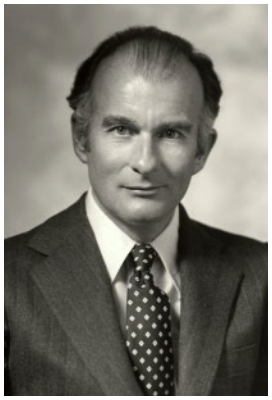
On a recent visit to NIH, he said retirement has already brought with it a number of surprises, like revealing his skill and passion for fine carpentry, a growing appreciation for the harmonica and requests for him to speak on the relationship of science and religion.

Anderson referred to his time at NIH as "a front-row seat for the most exciting show on Earth—the unfolding of human creativity and discovery in biomedical science." From the sounds of it, he's now producing and starring in his own show.

APAO Presents Annual Awards

The NIH Asian and Pacific Islander American Organization (APAO) held its annual awards ceremony recently. Debra Chew (l), director of the Office of Equal Opportunity and Diversity Management, gave the keynote speech at the ceremony. APAO vice president Dr. Eric Zhou (r) and Dr. Rashmi Gopal-Srivastava (second from r), chairman of APAO award committee, presented the scientific achievement awards to Dr. Wanjun Chen (third from r) of NIDCR and Dr. Vinay K. Pathak (second from l) of NCI and the Leadership Excellence Award to Dr. Francisco S. Sy (third from l) of NIMHD.

PHOTO: RUBY LEE



NINDS Mourns Retired Scientist Webster

Dr. Henry "Harry" de Forest Webster, retired chief of the NINDS Laboratory of Experimental Neuropathology, died at home in Cockeysville, Md. on Nov. 16, 2012.

Webster received his M.D. degree from Harvard Medical School and trained in neurology at Massachusetts General Hospital. After serving on the faculty at Harvard and the University of Miami medical schools, he was recruited to NIH in 1969 as chief of the section on cellular neuropathology at NINCDS (now NINDS). Webster was appointed chief of the Laboratory of Experimental Neuropathology in 1984 and held that position until 1997, when he became scientist emeritus. He continued to serve as a scientific mentor until his departure in 2009, taking a particular interest in the careers of women scientists.

During his career, Webster published many papers and received numerous awards and honors including the Alexander von Humboldt Foundation's Senior U.S. Scientist Award, to do research in Germany with German scientists, and the American Association of Neuropathologists' Meritorious Contributions to Neuropathology Award in 2001.

Webster began his scientific research when electron microscopy was first applied to the nervous system. He quickly became a master of the technique, using it to show how the myelin sheath forms and how it is disrupted in disease. Among his discoveries was a growth factor that could limit immune cells from entering the brain and attacking the glial cells that make myelin. His work advanced knowledge of the autoimmune basis of multiple sclerosis and contributed to the development of a variety of approaches to dampen the immune system to treat multiple sclerosis.

One of his most lasting contributions was the compilation of electron micrographs in *The Fine Structure of the Nervous System*, which he co-authored with Drs. Alan Peter and Sandy Palay. "Many generations of graduate students, including myself, viewed this as an essential reference," said NINDS director Dr. Story Landis.

Outside the laboratory, Webster applied his considerable darkroom skills—gained through electron microscopy—to photography, particularly of natural landscapes. He exhibited them at shows and often gave his prints as gifts. His colleagues noted that he had an excellent sense of humor and would often play the devil's advocate. "His quirky sense of humor and often contrarian viewpoint made many of us in Bldg. 36 pleased when we ran into Harry in the hallways," said Dr. Brian Andrews. "He would go off on some topic out of left field, but nonetheless interesting. These were great conversations."

Webster's wife of more than 60 years, Marion Havas Webster, died in 2012. Their survivors include 5 children and 6 grandchildren.—**Shannon E. Garnett**

Above, NIDDK's Dr. Benjamin Burton in 1978; at right,he conducts research earlier in his NIH career.

PHOTOS COURTESY AUDREY SOLNIT

NIDDK Scientist Emeritus Burton Dies at 93

Dr. Benjamin T. Burton, 93, who retired as NIDDK associate director for disease prevention and technology transfer and was named scientist emeritus in 1995, died Dec. 22, 2012. He had Alzheimer's disease.

At NIH for more than 34 years, Burton helped develop protein supplements to fight malnutrition in developing countries and played a major role in developing new technology for kidney dialysis. His textbook *Human Nutrition* has been translated into Spanish, Portuguese and Arabic.

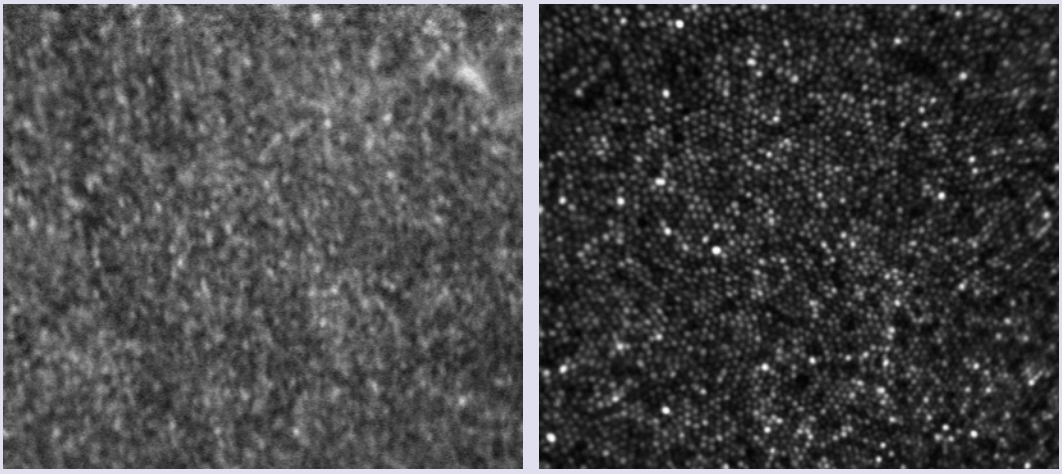
Born in Germany, Burton was reared in what is now Israel. He came to the United States to study at the University of California, Berkeley. He earned a Ph.D. in 1947.

In 1960, Burton joined NIH and began studying kwashiorkor, or protein-deficiency malnutrition. By 1965, he and his colleagues were working on kidney dialysis, developing workable and clinically effective artificial kidneys and methods for treating end-stage renal disease.

In 1995, he retired from NIH but not from science, noting, "I retired because it's decent to leave at 75, but I don't intend to stop what I've been doing. My goal is to continue doing something useful."

His daughter, Audrey Solnit, said he was true to his word. "Ben Burton loved NIH and continued to go to his office there 3 or 4 times a week until 2003," she said. "If Alzheimer's hadn't stolen my father's ability to drive to NIH and find his scientist emeritus office, he probably would have died at his NIH desk at 93."

In addition to Solnit, who lives in Morris, Conn., Burton is survived by son David Burton of Altadena, Calif., and 4 grandchildren.



Retinal images taken with scanning laser opththalmoscopy without (l) and with (r) adaptive optics (AO); AO reveals individual photoreceptors.

PHOTOS: JOSEPH CARROLL AND ALFREDO DUBRA, MEDICAL COLLEGE OF WISCONSIN

Technology for Stargazers Helps Scientists See Into Eye

By Dustin Hays

In the 1990s, astronomers pioneered a new technology—called adaptive optics, or AO—to help reduce distortion caused by the atmosphere when they looked at stars and planets through Earth-stationed telescopes. Now, vision researchers are using the same technology to reduce distortion caused by imperfections in the eye's cornea and lens when using light-based devices to look at the retina, the layer of light-sensitive tissue in the back of the eye. The retina houses rod and cone photoreceptors, which are specialized neuronal cells that convert light that enters the eye into electrical signals sent to the brain.

The National Eye Institute recently sponsored a workshop to explore how AO could be incorporated into clinical devices, giving more researchers and eventually eye care professionals access to this powerful technology that can noninvasively capture images of cells 20 times smaller than the diameter of a human hair.

For applications in the eye, AO works by aiming a dim beam of light toward the retina and then measuring distortion in the light reflected with a device called a wavefront sensor. Information collected by this sensor is read by a computer-controlled mirror that corrects the distortion before the light is viewed by the user. AO technology has been incorporated into a variety of imaging techniques, including optical coherence tomography and scanning laser ophthalmoscopy. The results are images with unprecedented sharpness.

"With adaptive optics, some of these high-resolution imaging techniques may provide us with an opportunity to identify early manifestations of disease that are not obvious with standard clinical tools," said Dr. Jacque Duncan, director of the University of California, San Francisco, retinal degenerations clinic, who helped plan the workshop. Such diseases include glaucoma, age-related macular degeneration and diabetic retinopathy—the three most common causes of vision loss among Americans.

The Clinical Application of Adaptive Optics Retinal Imaging incubator meeting, held at the headquarters of the Optical Society of America in Washington, D.C., explored key design parameters for clinical AO devices, including minimum resolution, ability to integrate with other imaging modalities, cost, portability and ease-of-use. The meeting heard perspectives from scientists and clinicians with diverse interests and requirements. In addition, representatives from Canon, Nidek, Topcon and other companies provided insight from a device manufacturer's perspective.

Workshop participants identified potential FDA requirements for AO devices used in standard clinical care and for use in clinical trials, which AO imaging could vastly accelerate. Many degenerative eye diseases, such as retinitis pigmentosa, cause vision loss over a period of many years due to a loss of photoreceptor cells. Subtle changes in vision are difficult to measure. AO would allow researchers to easily count rods and cones, providing a more objective means to evaluate a new therapy's effectiveness.

Participants identified several aspects that must be addressed before AO devices can be successfully integrated into clinical settings, including the need for standardized calibration protocols, defined metrics to gauge image quality and a reference database of "normal" samples. Several working groups were created at the meeting to address these aspects.

Dr. Matt McMahon, NEI senior advisor for translational research, said that standard and joint grant funding mechanisms and challenge prize competitions would help drive innovation in areas where AO technology is lagging, such as computer algorithms to automate photoreceptor cell counting.