

nih record



ABOVE • Dr. Hui Chen demonstrates Chinese calligraphy at a recent Ethnic Food Fair celebrating Asian heritage. Read more on p. 11.

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Thinning the Herd

The Battle to End Antibiotic Use in Farm Agriculture

By Dana Steinberg

During his 1945 Nobel Prize acceptance speech, Sir Alexander Fleming—who'd inadvertently discovered penicillin—warned against misusing antibiotics. “It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body,” he said. “There is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug, make them resistant.” Despite this foreshadowing, Fleming’s cautionary words went unheeded for decades.

While antibiotics have been a life-saving modern miracle, antibiotic resistance has threatened the existence of this precious commodity. The global widespread use of antibiotics in livestock has propagated this threat by breeding antibiotic-resistant microbes that can infect and kill people while rendering these drugs ineffective at treating the infections they were designed to cure.

“Even allowing for how new the antibiotic era was and how new these drugs were, and for the incredible enthusiasm with which they were being pursued around the

SEE **ANTIBIOTICS**, PAGE 6



Maryn McKenna gives a recent NLM History of Medicine Lecture.

A Technology Turnaround

Australian Scientist Goes from Bionic Ear To Bionic Eye

By Robin Latham

Thirty-six years ago, when Australian scientist (and 2013 Lasker Award winner) Dr. Graeme M. Clark did the first multi-channel cochlear implant in a human subject, it marked the beginning of a new method to treat people who had lost their hearing as a result of congenital deafness, injury or disease. Since then, more than 300,000 people worldwide have been fitted with a cochlear implant, including infants who are now allowed to be implanted as early as 6 months. This success has helped spur the development of other devices that substitute for lost motor, sensory or cognitive function such as neuromodulation devices that treat chronic pain and deep brain stimulators that reduce tremor and muscle rigidity in Parkinson’s disease.

Recently, the NEI International Vision Research program, along with the Fogarty

SEE **BIONIC EYE**, PAGE 8

Suicide Notes

New Studies May Help Us Understand, Predict Suicidal Thoughts, Behavior

By Dana Steinberg

Why do people consider killing themselves? What makes people transition from thinking about suicide to acting on it?

Nearly 1 million people die by suicide worldwide each year, according to the World Health Organization. That’s about 1 suicide every 40 seconds. In the United States, 38,000 people kill themselves annually. Nationally, suicide is the 10th leading cause of death and the third leading cause among adolescents and young adults. Yet despite public and private investments in sui-



Harvard University’s Dr. Matthew Nock

SEE **SUICIDE**, PAGE 4



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NIH...Turning Discovery Into Health

briefs

18th Annual Free Outdoor Film Festival

The 18th annual Comcast Film Festival will take place Aug. 15 - 17 at the MCPS Board of Education in Rockville. Teens and adults who are willing to give some of their time to help out from 4:30 to 9:30 p.m. for one night or a few nights are needed.

This year's films will be:

Friday, Aug. 15 *The Lego Movie* – PG

Saturday, Aug. 16 *Gravity* – PG-13

Sunday, Aug. 17 *The Hunger Games: Catching Fire* – PG-13

R&W can authorize community service, however it would prefer high schoolers. For details on volunteering, contact Kallie Wasserman at wassermank@mail.nih.gov.

Credit Union Opens Branch, Upgrades Service

The NIH Federal Credit Union will open its latest paperless branch this summer. The branch will be located at the new National Institute of Allergy and Infectious Diseases facility on Fishers Ln. in Rockville. The branch, accompanied by a full-service ATM, will be open Monday-Friday, 9 a.m.-4 p.m.

In late August, the NIHFCU will be upgrading its infrastructure so that it can serve its more than 40,000 members with the highest level of safety and security and deliver enhanced service options in the future. As a result of this system-wide upgrade, many member services will be temporarily disrupted from 10:30 p.m. on Friday, Aug. 22 through Sunday, Aug. 24. This includes branch closures, ATM withdrawal and debit card purchase limitations and online & mobile banking availability. NIHFCU members are encouraged to visit nihfcu.org/ServiceUpdate for more details so they can plan ahead to accommodate their transactional needs during this time.

Summer Poster Day Set, Aug. 7

Summer Poster Day 2014 is scheduled for Thursday, Aug. 7 at Natcher Conference Center from 9 a.m. to 3 p.m. Poster Day lets summer interns share the research they have been conducting and develop communication and networking skills. Any summer intern working in an intramural research group at NIH may present. Investigators, staff scientists and scientific administrators can make an important contribution to Summer Poster Day by visiting posters and engaging authors in discussion. For details, visit https://www.training.nih.gov/summer_poster_day.



NIDA Director Participates in World Science Festival

NIDA director Dr. Nora Volkow (r) recently attended the World Science Festival in New York City. She participated in The Brain and Addiction live event, which brought together leading scientists to discuss the big issues and latest developments in the fields of addiction neuroscience. She also participated in The Brain and Addiction Salon event, which more deeply explored the topics raised during the main program. Volkow's remarks centered around the effects of drug abuse on the brain, neuroscience, brain-imaging techniques and current research. She is shown above with NIDA grantee Dr. Eric Nestler.

Safety, Health, Wellness Day, Aug. 27

The NIH Safety, Health and Wellness Day will be held Wednesday, Aug. 27, rain or shine, at the Natcher Conference Center from 10 a.m. to 2 p.m. Everyone is welcome to come and enjoy the activities and learn about safety, health and wellness opportunities at NIH. The Office of Research Services, Office of Research Facilities, NIH occupational safety and health committee, IC safety and health chairpersons committee, laboratory sustainability group and the National Human Genome Research Institute are combining efforts to increase workplace health awareness and promotion.

The focus of this year's event is to enhance employee nutrition, wellness, physical fitness, safety awareness and prevent or reduce work-related injuries and illnesses. A wide range of activities and exhibits will be presented including health screenings, nutrition demonstrations and tastings, physical fitness activities, NIH IC exhibits and heart-saver CPR training.

Over 50 exhibitors, including federal agencies such as the Occupational Safety and Health Administration, Centers for Disease Control and Prevention, Food and Drug Administration and the Defense Intelligence Agency, will showcase nutrition, fitness and occupational health and wellness information and activities.

Plan to stay for lunch and choose from a menu that will include special healthy choices. For more information, visit <http://go.usa.gov/XYRm>.

Individuals who need reasonable accommodation to participate should contact Carole Harman at (301) 402-8180 and/or the Federal Relay at 877-709-5798. A special shuttle route will run between Bldgs. 10 South, 40 (to service Bldgs. 29, 30, 35, 37, 40 and 49) and the Natcher Conference Center from 10 a.m. to 2 p.m. For staff located off-campus, there will be free parking in the MLP-11 (visitor) parking garage off Rockville Pike during the event.

nih record



Dr. Sherry Glied of New York University

Glied Talks Affordable Care Act, Mental Health Parity at NIMH Outreach Meeting

By Keri Chiodo

Representatives from mental health organizations across the country recently came to NIH for the 15th annual meeting of the NIMH Outreach Partnership Program. The OPP is a nationwide network of 55 state mental health organizations representing all states, the District of Columbia and Puerto Rico that aims to deliver science-based mental health information to the public.

The meeting is an opportunity for partners to share ideas with each other and representatives from more than 80 national organizations, as well as learn about the latest research and policy advances from NIMH scientists and thought leaders.

Dr. Sherry Glied, dean of the Robert F. Wagner Graduate School of Public Service at New York University, gave the keynote address, Implementing Mental Health Parity in the Current Health Care Paradigm.

“Dr. Glied is, without question, one of the national experts, if not the national expert on mental health parity reform,” said NIMH director Dr. Thomas Insel. “She was right in the center of this historic shift in the way that services would be provided in this country.”

Glied was confirmed by the U.S. Senate as assistant secretary for planning and evaluation for the Department of Health and Human Services in 2010. During her 2-year tenure, she ensured that policies for coverage of mental health and substance use disorders were on par with those for other medical conditions in the Affordable Care Act.

“The interesting thing about the ACA is that it hardly mentions mental health or substance

abuse at all, and yet it is likely that the ACA will have a tremendous effect on mental health and substance abuse provisions, access, financial availability and even on the way care is provided,” Glied said. “The impact of this law on people with mental illness is actually much bigger than it is for the population overall.”

To put the ACA into perspective, Glied described how changes in federal policies and programs over the past several decades unintentionally benefited people with mental illness.

“Back in 1957, if you were not actually hospitalized in a psychiatric institution, there was very little chance you were going to get any mental health services anywhere else,” Glied noted. By the 1970s, an expansion in social programs such as social security disability benefits improved the lives of people with serious mental illness. The share of people who received mental health services also increased due to a growth of insurance-based health care financing.

Glied noted that it took two failed attempts at comprehensive federal health care reform by both the Nixon and Clinton administrations and over a decade of advocacy and research efforts that eventually led to mental health parity legislation in 2008. This required that private insurance plans that included any mental health benefits provide those benefits in the same manner as all other health benefits.

Health care coverage under the ACA will provide what Glied calls “parity plus”—wherein mental health benefits are officially considered essential health benefits. The ACA will also expand people’s access to affordable services and treatments. Glied estimates that when the ACA is fully in place, 30 million people who were previously uninsured or underinsured will gain mental health benefits.

“This is a critical area for mental health advocacy,” Glied told the audience. She proposed that mental health workers and advocates could help shape the future of the ACA by monitoring its effects within their own communities, in terms of financial burden, access to care and stigma. 🗣️

6100 Exec. Blvd. Reopens

The NIH leased office building at 6100 Executive Blvd. in Rockville has reopened after a structural problem at the building on May 16 temporarily closed the facility. Water damage to a structural column caused the building to shift slightly on the morning of May 16. No one was injured, but Montgomery County closed the building for several weeks.



“The safety of NIH staff has been and will remain of paramount importance,” said Brad Moss, spokesman for the Office of Research Facilities, just prior to the building’s re-occupation. “The remediation of the building is being accomplished under the direct supervision of the owner’s structural engineer, with oversight by the Montgomery County department of permitting services as well as an independent structural consultant engaged by NIH.”

ORF held an all-hands session July 1 in Natcher Conference Center for tenants of 6100, who were invited to ask questions or raise concerns about the safety of the building. Montgomery County removed its unsafe notice from the building on Monday, July 7 and re-occupancy began on Tuesday, July 8 for employees from OD, the Clinical Center and NICHHD.

SUICIDE

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Nock says, "Suicide is a huge problem for us philosophically, clinically, scientifically and as a society. It's something we really need to try to do a better job of understanding."

PHOTOS: ERNIE BRANSON

cide research, U.S. suicide rates have not noticeably decreased in decades, which signals a need for better methods to predict and prevent self-injurious intent and behavior.

"Suicide is a huge problem for us philosophically, clinically, scientifically and as a society," said Dr. Matthew K. Nock, professor of psychology and director of the Laboratory for Clinical and Developmental Research at Harvard University. "It's something we really need to try to do a better job of understanding."

Studies of suicide risk typically rely on retrospective self-reporting, which limits our ability to observe what triggers suicidal thoughts and how long they may last, argued Nock, who spoke at the NIMH Director's Innovation Speaker Series recently. While we can cull important data and trends from these studies, he advocates the need for studies that reveal self-injurious intentions in real time.

Suicidal thoughts, or ideation, can be hard to measure. Such thoughts often are transient and patients might not reveal them during clinical exams. Also, people tend to deny or contain thoughts of suicide, said Nock, which may help explain why there's such a spike in suicide deaths shortly after at-risk patients are discharged from a hospital.

One of the largest studies on suicidal behavior, the WHO World Mental Health Survey Initiative, which is funded in part by NIMH, is providing data on suicidal thoughts, plans and attempts across a large, nationally representative sample.

About 10,000 Americans were interviewed at length in their homes; the study is being replicated in more than 25 countries.

Based on responses from 85,000 adults in the 17 countries for which data has been analyzed, 9 percent of respondents have seriously considered killing themselves, 3 percent made suicide plans and almost 3 percent made attempts.

Rates are among the highest in the U.S., where 15 percent of adults reported having suicidal thoughts, 5 percent made suicide plans and 5 percent made attempts.

The findings look fairly consistent cross-nationally. Men are 4 times more likely to die by suicide in every country examined. Also, suicide risk is higher for those who are younger, unmarried or have mental disorders.

A prior mood disorder corresponded to a 4- to 6-fold increase in the odds of suicide ideation, plans or attempts. Interestingly, those suffering from depression were more likely to have suicidal thoughts but not to act on them. Nock said people with disorders char-

acterized by agitation, anxiety, poor behavioral control or substance abuse were more likely to act on their suicidal thoughts.

Similarly, a family history of depression or anxiety predicted onset and persistence of ideation but did not necessarily predict actions. Those whose parents had a history of panic or antisocial behavior had a higher risk of acting on their suicidal thoughts.

In this study, about one-third of people who had suicidal thoughts actually made a suicide plan or suicide attempt.

In every country examined, at least 60 percent of transition to suicide attempts happened within the first year after onset of ideation, said Nock. And consequently, the longer someone goes thinking about suicide without making a suicide attempt, the less likely that person is to make a suicide attempt.

Additional data show that about half to two-thirds of adolescents with ideation, plans or attempts were in treatment prior to onset. "As a society, we're doing a good job of capturing those at risk and getting them into treatment before they become suicidal," said Nock. "On the flip side, [despite treatment], they're still thinking about suicide and making suicide attempts."

While such studies reveal important clues to understanding the suicidal mind, Nock's team is working to introduce more real-time monitoring studies to help assess self-destructive thoughts and behaviors as they occur among at-risk adolescents and young adults.

In one study, 30 adolescents ages 12-19 with a recent history of non-suicidal self-injury were asked to log entries into electronic diaries regularly for 2 weeks. Respondents reported thinking about self-injury more frequently and with greater intensity than they thought about suicide. About one-fifth of those who thought about self-injury also thought about drinking and drug use at the same time but weren't actually drinking or using drugs at the time. Many reported feeling sad or overwhelmed during ideation. But those who reported feeling rejected, angry or self-hatred were the ones who made plans or attempts at self-injury.

While the sample size is small, this type of study can be an important tool in helping to identify markers of imminent risk. Current research is aimed at developing new cognitive tests and new interventions to decrease suicidal thinking.

There's a great need, said Nock, to develop innovative ways to measure risk to ultimately improve suicide assessment and treatment. 🗨

National Climate Assessment Addresses Human Health

NIEHS helped develop the recently released health-related aspects of the Third National Climate Assessment (NCA). The assessment emphasized that climate change, once considered an issue for the distant future, has moved firmly into the present, with impacts on human health.



Dr. John Balbus was recently awarded an HHS Green Champions Award for developing the Sustainable and Climate Resilient Healthcare Facilities Initiative, released June 2013, as part of the President's Climate Action Plan.

PHOTO: STEVE MCCAWE

“The real importance of this NCA report, compared to the previous two, is that it is very much oriented to the general public,” said NIEHS senior advisor for public health Dr. John Balbus, a lead author for the human health chapter. “People are much more engaged than with previous assessments.”

As part of the strategy to reach a more general audience, the report’s web site, www.globalchange.gov,

is deliberately visual and interactive, with graphics and short summaries of key points, noted Balbus. The extensive media attention the report received often emphasized health, such as the effects of climate change on allergens, asthma and vector-borne diseases.

The chapter on health includes messages on impacts that range from changes in disease-borne illness, such as through the expanding range of the tick that carries Lyme disease, to impacts of decreased air quality, threats to vulnerable populations and public health actions that can help protect from existing and emerging threats.

The NCA focuses on the U.S., but makes clear that climate change is a global health problem. As a World Health Organization Collaborating Centre for Environmental Health, NIEHS is sharing the findings with counterparts in other countries.—Paula Whitacre



NINR director Dr. Patricia Grady (c) and AACN summit participants

Grady Emphasizes ‘Translational Science’ at AACN Summit

“Clinical and translational science, led by nurses, is central to the reform movement in health care,” NINR director Dr. Patricia Grady told the audience at the recent American Association of Colleges of Nursing (AACN) Student Policy Summit. “This demonstrates not simply the incredible power of scientific research and discovery as a positive change agent, but also illuminates the responsibility we have as clinical and translational scientists to effectively disseminate our scientific findings to our practice and policy communities.”

The 3-day conference, held in Washington, D.C., brought together an interdisciplinary audience of nursing students and leaders in academia, research, clinical practice and policy. Grady spoke about health care system challenges—such as the rising demand for clinicians, an aging population, the demand for lower costs and how “nurse scientists are leading the way in discovering and implementing solutions to these challenges.”

In one example Grady offered, NINR-supported researchers demonstrated that nurse-managed transitional care reduced hospital readmissions and total health care costs. To disseminate and translate their findings, the researchers formed partnerships with clinicians and major health insurers. “It is a reciprocal translational continuum—research informs education, clinical practice and policy,” said Grady.

In addition to the lecture, Grady met with AACN faculty policy intensive fellows to talk about NINR research and training opportunities and the contributions of nursing science, which she said “illuminate the scientific path for policymakers faced with solving complex health challenges, resolving restricted budgets and advancing health system reform.”

Boyle Heads NIDA Science Policy Branch

Dr. Maureen Boyle has been named chief of the Science Policy Branch in the Office of Science Policy and Communications, NIDA. She comes from the Substance Abuse and Mental Health Services Administration, where she coordinated efforts to develop solutions for health IT challenges facing the behavioral health community in this era of health care reform.



Prior to joining SAMHSA, Boyle was a science and technology policy fellow with the American Association for the Advancement of Science serving at NIH’s Office of Behavioral and Social Sciences Research. She received her Ph.D. in neuroscience from Washington University in St. Louis, where she studied the genetic and molecular basis of depression and anxiety-related behaviors. She completed a post-doctoral fellowship at the Allen Institute for Brain Science, where she investigated neuropathological, molecular and genetic abnormalities in autistic children and animal models of autism.

Right: Antibiotics in art. Before the advent of antibiotics, in the late 19th century, scientists collected blood serum from animals to treat diphtheria, an often fatal childhood disease. This picture, drawn by Fritz Gehrke, shows serum taken from horse blood, in Marburg, Germany. The artwork is part of an NLM exhibit (see details below).



Above, McKenna with Dr. Jeffrey Reznick, chief of NLM's History of Medicine Division

ANTIBIOTICS

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Below: NLM's "From DNA to Beer: Harnessing Nature in Medicine & Industry" exhibit explores the problems and potential inherent in technologies that use microorganisms for health and commercial purposes. This image, "The Era of Antibiotics" by Robert A. Thom, was commissioned by Parke, Davis & Co., for its 1950s ad campaign, "Great Moments in Pharmacy." See the exhibit at www.nlm.nih.gov/exhibition/fromdnato-beer/index.html.

world, it's really surprising for me to look back and see the degree to which any evidence of possible unintended consequences was simply dismissed," said Maryn McKenna, senior fellow, Schuster Center for Investigative Journalism at Brandeis, at her recent NLM History of Medicine Lecture "Losing the Miracle: Agriculture, FDA and the Controversy over Farm Antibiotics."

Some 7.7 million pounds of antibiotics are sold to treat sick people in a single year in the U.S., based on 2011 International Monetary Fund data, McKenna reported. According to the FDA, nearly 30 million pounds were sold for use in meat-producing animals; most was given for growth promotion, not for therapeutic use, and with little oversight, she said.

The use of antibiotics in livestock dates back to the 1940s. Researchers searching for ways to make animal feed more efficient and less costly tried using the newly developed broad-spectrum antibiotic aureomycin, later to become chlortetracycline. In 1948, the researchers observed that chicks given aureomycin weighed three times as much as the others. Soon, penicillin and other antibiotics would also be used to fatten livestock and, in 1961, the Food and Drug Administration approved antibiotic use for growth promotion.

"That you can cause these animals to reliably gain weight faster on the same feed, or less feed, is something that was done incredibly quickly, so quickly in fact that there was almost no consideration of the [hazards]," said McKenna.

In the 1960s, the United Kingdom established the first government-supported committee to study antibiotic use in agriculture after people became seriously ill and some died from salmonella and *E. coli* poisoning linked to cattle farms. Around that time, FDA began to study the issue.

Over the years, concern intensified over the potential impact of animal antibiotics on human health. Veterinarians cautioned about putting even small doses of antibiotics into animals in

an uncontrolled environment, said McKenna. In fact, antibiotics used to promote growth in animals often were given at low levels over extended periods—known as sub-therapeutic dosing—creating the dangerous under-dosing scenario Fleming warned about nearly 70 years ago.

Then experimental proof started to surface that sub-therapeutic dosing of farm animals can threaten human health. In 1977, the Department of Health, Education and Welfare (later renamed the Department of Health and Human Services) responded by proposing to withdraw licenses for penicillin and tetracycline for growth promotion in animals, but the plan wasn't implemented.

Other groups began to echo their concerns, from county health departments to the National Academy of Sciences. Despite increasing public and political pressure and further research from health organizations, "The agriculture industry, which benefits from growth-promoting antibiotics that make meat less expensive to produce, is unpersuaded by any of the research and has been unpersuaded for decades," said McKenna.

In 2004, a curious case of resistance appeared on a farm in the Netherlands, which used more antibiotics in meat animals than any other EU country, said McKenna. A young girl tested positive for a drug-resistant staph infection (MRSA strain ST398), which unlike other MRSA strains was resistant to tetracycline. Interestingly, tetracycline wasn't used to treat human MRSA in the Netherlands but was used routinely in pigs. That means the only place this strain could've developed its unique resistance pattern was in pigs, said McKenna. This case also reinforced that resistant bacteria generated by antibiotic use on farms can move off farms and infect people with no connection to farming.

In 2006, the EU banned antibiotics as growth promoters in animals. The U.S. took a different approach. In 2010, the FDA asked the veterinary pharmaceutical sector to voluntarily stop using antibiotics in animals for food production purposes.



es. After a follow-up, Guidance 213, issued last December, 25 of 26 U.S. pharmaceutical manufacturers told the FDA they'd comply and change their labeling.

Neither the U.S. voluntary guidance nor the EU ban addresses or regulates antibiotics given to farm animals for disease prevention and control purposes, noted McKenna. It's also unclear whether U.S. companies will continue to comply with the FDA's voluntary directive.

The true test will be whether we see a real decrease in antibiotic-resistant infections in animals and people. The less antibiotics are used overall, the greater the chance to help protect these drugs so they keep working to save lives across the world. 📌

Bare Named CSR Executive Officer

Joanna Derksen Bare has been named executive officer at the Center for Scientific Review.



She will lead the efforts of staff and contractors who provide administrative, financial management, committee management, procurement and management analysis services that enable CSR to fulfill its mission.

Each year, the center receives over 80,000 grant applications, engages more than 17,000 reviewers from the scientific community and hosts about 1,500 electronic and face-to-face review meetings.

"Joanna brings to CSR an incredible set of people and management skills," said CSR director Dr. Richard Nakamura. "She is known for building and leading successful teams at NIH that excel in challenging times. She also has a unique scientific and engineering background, which will help her better understand and work in a scientific organization."

Bare holds master's degrees in industrial engineering and physics from the University of Washington and a B.A. degree in physics from Carleton College.

She comes to CSR from the NIH Office of Research Facilities, Division of Facilities, Operations and Maintenance, where she was deputy director and, earlier, chief of its Project Control Office. Prior to this, Bare worked at Management Analysis, Inc., in Vienna, Va., where over the course of 12 years, she rose from being an industrial engineer to being a project manager and corporate secretary.

First CRC Patient's Genetic Disease Unraveled

By Eric Bock

Clinical Center researchers have identified the genetic defect underlying the disease for the first admitted patient at the Hatfield Clinical Research Center.

The patient has Carney complex, a rare genetic disorder that affects 700 people. People with Carney complex often have skin pigmented spots resembling freckles, over-active endocrine glands that produce too many hormones and a number of different types of benign and cancerous tumors.



NICHHD's Dr. Constantine Stratakis (fourth from r) and his colleagues

The patient was enrolled in a research protocol of Dr. Constantine Stratakis, director of the Division of Intramural Research and head of the section on genetics and endocrinology at NICHHD. He said the discovery of the new defect will provide the basis for efforts to screen patients with Carney complex with similar defects. Ultimately, he hopes that discovery of the defect will lead to effective treatments for Carney complex.

"There are hundreds of ongoing studies just like this one at the Clinical Center," said CC director Dr. John Gallin. "In understanding rare diseases, we not only are in a position to help those who have the diseases, but often we identify new gene or protein targets for the discovery of new therapeutics relevant to common diseases. Thus, in addition to providing hope to the patients with the rare disease we often can apply what we learn to a variety of other diseases and conditions as well."

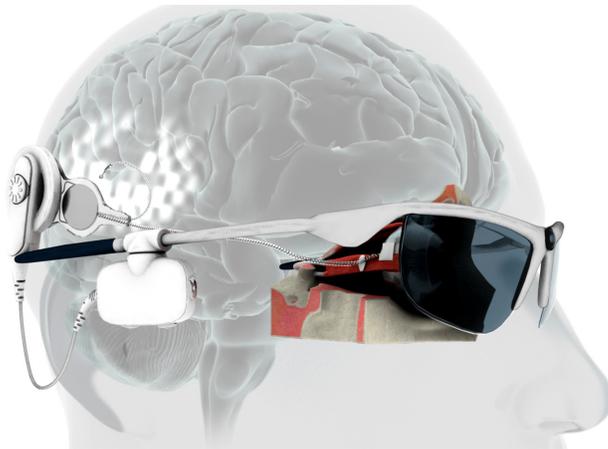
On Apr. 3, 2005, the first patient admitted to the CRC enrolled in Stratakis's protocol. Then, Stratakis thought the patient had Carney complex, but lacking a definitive test, he couldn't confirm the suspected diagnosis. However, he continued to follow the patient's progress through the years at the Clinical Center.

"Nine years ago, we didn't have the technology to identify the disease's genetic defect," Stratakis said. "As technology advanced, we were able to find it. Patients we thought didn't have [Carney complex] turned out to actually have it. It's amazing how far genetic technology has come."

In 1994, Stratakis set up a program at the CC to study patients with adrenal and pituitary tumors. This research led him to study Carney complex or suspected Carney complex, a genetic syndrome that affects both the pituitary and the adrenal glands. Since then, he estimates he's diagnosed the condition in 400 to 500 patients.

Including the gene for the first patient at the CRC, so far he's identified three genetic defects resulting in Carney complex and at least two others that may contribute to the disease's development, at least with regard to adrenal tumors. Stratakis's laboratory has identified several other genetic defects that cause pituitary or adrenal tumors in patients with other conditions such as multiple endocrine neoplasias, cancer, gastric stromal tumors, pheochromocytomas or paragangliomas.

"I'm confident that understanding the genetic basis of the Carney complex will lead to a treatment that targets the cause of the disease," Stratakis said. "Just because we don't have a treatment yet doesn't mean we won't find it in the days, months and years ahead."



BIONIC EYE

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Above, from l:

Longtime NIH grantee Dr. Robert Shepherd is now director of the Bionics Institute of Australia and head of the medical bionics department at the University of Melbourne.

Seeing into the future. *A graphic of the next-generation bionic eye developed by Shepherd's team*

IMAGE: BIONICS INSTITUTE

International Center and the NIH global health interest group, hosted a talk by a scientist on Clark's original team, Dr. Robert Shepherd, a longtime NIH grantee who is now director of the Bionics Institute of Australia and head of the medical bionics department at the University of Melbourne. The institute and its research partners in Bionic Vision Australia were recently awarded a \$10 million grant from the Australian government to further develop a visual prosthesis, or "bionic eye," to restore useful vision to blind patients.

There are many other groups worldwide working on the problem of a retinal prosthesis, but Shepherd's approach is to modify the electrode array and stimulation technology that were developed for the cochlear implant. "The cochlear implant is a mature technology," said Shepherd. "We thought we could take advantage of the knowledge of 30-plus years of research and apply it to a different sensory system using tried-and-true materials that have already been shown to be safe to use in clinical research."

Visual prostheses currently under development in different labs are designed to restore vision by stimulating nerve cells at different sites along the visual pathway. These include the retina (the eye's light sensor), optic nerve (the connection from the eye to the brain) and visual cortex in the brain. But Shepherd believes that stimulating just behind the retina, rather than along the optic nerve or in the visual cortex, takes advantage of the eye's built-in circuitry for transforming light into an image.

"This means the natural organization of the eye and the central visual pathway is doing some of the heavy lifting of creating an image perception," says Shepherd. "We've found that neural pathways in the eye are still intact, even after as many as 20 years of blindness."

The device Shepherd's team is developing includes an external video camera, a vision processor, power supply and an implanted stimulator. The stimulator connects to an electrode microarray surgically implanted behind the retina between two layers of the eye, the sclera (the white part) and the choroid (a blood vessel layer). This is called a suprachoroid

implant. Based on extensive preclinical studies already performed by the group, Shepherd theorizes that it will provide a safer and simpler surgical implant procedure, as well as a more mechanically stable location, compared to subretinal or epiretinal implants.

This prototype bionic eye has been successfully implanted in three blind volunteers in Australia, who had lost their vision due to retinitis pigmentosa, a condition that causes progressive vision loss often starting in adolescence. Because there are only 24 electrodes in the microarray while the retina contains millions of neurons, the device provides low-resolution vision, what is sometimes called "shape vision." It doesn't allow the user to see a detailed visual scene, but it can be helpful for navigation. Wearing the device, one volunteer was able to walk through a room and avoid obstacles without her guide dog for the first time in 20 years.

At the end of the lecture, Shepherd screened a video of one of the participants who admitted that what she was seeing wasn't like regular vision, but she was learning to trust what she saw. "It's been amazing," said Dianne Ashworth. "The more I've been doing it, the more natural it feels."

Up next for Shepherd's team is a fully implantable device using 44 electrodes to improve image resolution, along with another piece of technology to aid in the patient's depth perception. They expect to implant this device in an additional 3 to 6 patients. Shepherd hopes that additional steps will occur in the near future for good restoration of vision in blind or visually impaired people. He emphasized the importance of multidisciplinary research in achieving these technological advances: "This work is only successful because of an effective research team including eye specialists, scientists and engineers who are focused on developing the technology.

"In 5 years, I think there will be 2 or 3 visual prosthetic devices that will be considered the standard of care for conditions such as end-stage retinitis pigmentosa, and we'll also be expanding the research into other areas of vision pathology," he concluded. 

digest

Study Identifies Novel Genomic Changes in the Most Common Type of Lung Cancer

Researchers from The Cancer Genome Atlas (TCGA) Research Network have identified novel mutations in a well-known cancer-causing pathway in lung adenocarcinoma, the most common subtype of lung cancer. Knowledge of these genomic changes may expand the number of possible therapeutic targets for this disease and potentially identify a greater number of patients with treatable mutations because many potent cancer drugs that target these mutations already exist.

In the study, published online July 9 in the journal *Nature*, researchers examined the genomes, RNA and some protein from 230 lung adenocarcinoma samples. In three-quarters of the samples, the scientists ultimately identified mutations that put a cell signaling pathway known as the RTK/RAS/RAF pathway into overdrive.

“The integrated nature of TCGA analysis made these findings and their potential therapeutic implications possible,” said NIH director Dr. Francis Collins. “We hope this lays the groundwork for future work in precision medicine.”

Mutations affecting the RTK/RAS/RAF pathway can cause it to become stuck in the “on” state. As a result, signals that promote cancer cell proliferation and survival are produced continuously. However, some drugs currently available curb aberrant activity of this pathway and prompt therapeutic responses in patients.

Lung adenocarcinoma, the most common form of the disease in the United States, develops in tissues near the outer parts of the lungs and can spread widely.

NIH Study Finds Extreme Obesity May Shorten Life Expectancy Up to 14 Years

Adults with extreme obesity have increased risks of dying at a young age from cancer and many other causes including heart disease, stroke, diabetes and kidney and liver diseases, according to results of an analysis of data pooled from 20 large studies of people from 3 countries. The study, led by researchers from NCI, found that people with class III (or extreme) obesity had a dramatic reduction in life expectancy compared with people of normal weight. The findings appeared July 8 in *PLOS Medicine*.

“While once a relatively uncommon condition, the prevalence of class III, or extreme, obesity is on the rise. In the United States, for example, 6 percent of adults are now classified as extremely obese, which, for a person of average height, is more than 100 pounds over the recommended range for normal weight,” said Dr. Cari Kitahara of NCI’s Division of Cancer Epidemiology and Genetics and lead author of the study. “Prior to our study, little had been known about the risk of premature death associated with extreme obesity.”

The 20 studies that were analyzed included adults from the United States, Sweden and Australia. The researchers found that the risk of dying overall and from most major health causes rose continuously with increasing BMI within the class III obesity group.

NIH Scientists Identify Gene Linked to Fatal Inflammatory Disease in Children

Investigators have identified a gene that underlies a very rare but devastating autoinflammatory condition in children. Several existing drugs have shown therapeutic potential in laboratory studies and one is currently being studied in children with the disease, which the researchers named STING-associated vasculopathy with onset in infancy (SAVI). The findings appeared online July 17 in the *New England Journal of Medicine*. The research was done at NIAMS.

“Not only do these discoveries have profound implications for children with SAVI, but they could have a broader impact by helping us to understand other, more common inflammatory conditions,” said NIAMS director Dr. Stephen Katz. “Diseases such as lupus share some characteristics with SAVI, so this work may lead to novel insights and possibly new treatments for these debilitating conditions as well.”

The senior author of the study, Dr. Raphaela Goldbach-Mansky, and co-lead authors Dr. Yin Liu, Dr. Adriana A. Jesus and Dr. Bernadette Marrero are in the NIAMS translational autoinflammatory disease section.

In 2004, Goldbach-Mansky was called upon to advise on a patient with a baffling problem—a 10-year-old girl with signs of systemic inflammation, especially in the blood vessels, who had not responded to any of the medications her doctors had used to treat her. By 2010, Goldbach-Mansky had seen two other patients with the same symptoms. She suspected that all three had the same disease, and that it was caused by a genetic defect that arose in the children themselves, rather than having been inherited from their parents, who were not affected. Her hunch suggested a strategy for identifying the genetic defect. By comparing the DNA of an affected child with the DNA of the child’s parents, scientists would be able to spot the differences and possibly identify the disease-causing mutation.

“When mutations that cause autoinflammatory conditions hit an important pathway, the outcome for patients can be dismal,” said Goldbach-Mansky. “But because SAVI is caused by a single gene defect and interferon has such a strong role, I’m optimistic that we’ll be able to target the pathway and potentially make a huge difference in the lives of these children.”



NIAMS team members include (from l) Dr. Yan Huang, Dr. Bernadette Marrero, Dr. Adriana A. Jesus, Dr. Gina Montealegre, SAVI patient Elliot Schuman, Dr. Raphaela Goldbach-Mansky, Patricia O’Brien, Dawn Chapelle and Dr. Yin Liu.

NEI's Ferris, Chew Receive Keller Prize for Vision Research

Dr. Frederick L. Ferris III and Dr. Emily Y. Chew, who are director and deputy director of the NEI Division of Epidemiology and Clinical Applications, have received the Helen Keller Prize for Vision Research.

"It is a real honor to be chosen for the Helen Keller prize and it has been a tremendous privilege to work at the National Eye Institute with such a large group of brilliant collaborators on projects with major public health significance," said Ferris.

The award recognizes significant contributions to vision science; the Helen Keller Foundation for

Research and Education has bestowed it to one or two researchers each year since 1994.

Ferris and Chew received the award for their efforts to investigate new treatments for cataract, age-related macular degeneration (AMD) and diabetic eye disease through large, multi-center clinical trials.

For example, in a landmark trial, they helped establish that laser treatment can reduce the risk of severe vision loss by up to 95 percent in people with diabetic retinopathy, a common type of diabetic eye disease. They are also founding members of the Diabetic Retinopathy Clinical Research Network, which has enabled other large clinical trials on the condition by joining together nearly 1,000 investigators in 48 states. Ferris and Chew also launched—and continue to lead—the NEI Age-Related Eye Disease Studies (AREDS and AREDS2). These studies have found that certain high-dose antioxidants and minerals can reduce the risk of vision loss for people with AMD.

"I am extremely honored to receive this recognition. We are grateful to have had tremendous mentors. The Helen Keller prize is shared by our entire NEI team and collaborators involved in clinical epidemiologic research," Chew said.

Helen Keller laureates are selected by an international panel of experts. The prize ceremony took place in Orlando at the annual meeting of the Association for Research in Vision and Ophthalmology, which attracted more than 13,000 scientists and physicians this year.

NIBIB Mourns Lopez's Passing

Dr. Hector Lopez of the National Institute of Biomedical Imaging and Bioengineering died June 21. He had a distinguished career in government that lasted more than 40 years. He joined NIBIB early in its history—almost a decade ago—bringing his expertise in medical ultrasound imaging.

Prior to joining NIBIB, he worked for the Food and Drug Administration's Center for Devices and Radiological Health, where he conducted research in the development of methods and tools for the objective measurement of imaging system performance. His research also included development of innovative ultrasound imaging techniques and measurement methods in the body.

While diagnostic and interventional ultrasound, as well as x-ray, electron and ion beam were his areas of expertise, Lopez was well known for his extensive knowledge in many areas of imaging. Many at NIBIB relied on his sound analysis of a variety of scientific issues. A true physicist at heart, he was as likely to be found discussing the fundamentals of special relativity as the minutia of ultrasound technology. His unique intelligence and attention to detail will be greatly missed by his colleagues at NIBIB.

Lopez served in the Air Force and received the Air Force Commendation Medal for discovering a leaking radioactive source and his prompt, decisive action in initiating decontamination procedures. He received numerous awards during his time at FDA and participated in professional societies.

In 1995, he was elected fellow of the American Institute of Ultrasound in Medicine and served as chair of the AIUM technical standards committee from 1999 to 2001, as well as chair of working group 9 of the International Electrotechnical Commission from 1999 to 2004. He was also a member of the American Association of Physicists in Medicine.

Lopez is survived by his sister Gloria and brother Antonio.



At the Keller prize ceremony are (from l) Drs. Miriam and Frederick Ferris, Dr. Emily Chew, Keller Johnson-Thompson, who is the great-grandniece of Helen Keller, and Dr. Robert Murphy, who is Chew's husband.

feedback

Have a question about some aspect of working at NIH? You can post anonymous queries at www.nih.gov/nihrecord/index.htm (click on the Feedback icon) and we'll try to provide answers.

Feedback (two related queries): What's up (or not) with elevators 13 and 14 in Bldg. 10? First they shut them down for "repairs" last month and ever since they have not shown floor indicators (at all or correctly) like they should. Combine that with the fact that they seem to take their notions on whether or not to actually come when called and those of us stuck on the west side of the F-wing construction deal with daily elevator frustration just to fulfill the mission of NIH.

Is anybody maintaining the elevators in old Bldg. 10? Freight elevator #15 has been out of commission for months. With the finishing up of the F wing, the freight elevator will be needed to help in the moving in of equipment, etc. Elevator #37 is not working in the west tower. Many of the elevators do not have working floor indicators on the inside or outside of the elevators and one in the D section and [one in] the ACRF section don't have a noise indicator to let you know that the elevator has arrived. In the past, the elevators seemed to be constantly monitored, but now they seem to be ignored. What has changed?

Response from the Office of Research Facilities: ORF sympathizes with employee frustration associated with the elevators in Bldg. 10. There is a regular and vigorous maintenance program for the Bldg. 10 elevators and for all NIH elevators. Elevators (and escalators) are the most complex facilities systems that building occupants interact with. They are designed to default to safe operation over fast or efficient operations—which can sometimes make them frustrating to use and to maintain. Elevator problems often arise from something as simple as running into the elevator doors with a cart, which causes the doors and door safety features to become misaligned. When this occurs, the elevator will shut down rather than operate with doors that potentially do not close completely or correctly.

For elevators 13 and 14, maintenance staff had been experiencing significant issues with software that supports display of elevator locations

from inside the elevator cab. Although indicators in hallways functioned properly, corresponding indicators inside several elevator cabs were malfunctioning. Thankfully, a new software upgrade in July resolved the issue and the position indicators should function normally inside and outside the elevators.

Problems with freight elevator 15 were identified during its regular "5-year full load test." Every 5 years, these tests put the elevator through extreme performance conditions, including a full speed safety stop with the elevator loaded at 25 percent over its stated weight capacity. This is done to ensure that its safety devices function properly. During the test, freight elevator 15 showed specific signs of wear that require us to make repairs. Although we recognize the significant inconvenience to Bldg. 10 occupants, ORF is committed to the safety of everyone who uses elevators at NIH.

Employees and construction personnel can help to improve elevator response times by not selecting the call buttons for both pedestrian and freight elevators simultaneously, then taking whatever elevator arrives first. This common practice leads to delays and "ghost calls" when the second elevator arrives to a floor with no one waiting. This is particularly prevalent in the F wing, where the closure of hallways due to construction limits the number of elevator options. In addition, passenger elevators are specifically designed for the dynamic load of moving people. Freight elevators are designed for moving heavy loads. These design differences make it wiser for people to use passenger elevators unless they are transporting something that necessitates the use of a freight elevator. 🗣️



At the annual Ethnic Food Fair were (from l) Kausik Ray, JoAnne Wong, Aaron Bell, Tyrone Banks, Laura Wong, Chunzhang Yang, Mary Zhang, Phuong-Tu Le, Shioko Kimura and Donna Wells.

Annual APAO Food Fair Is a Success

The NIH Asian and Pacific Islander American Organization (APAO) recently held its annual Ethnic Food Fair on the patio of Bldg. 31A. Several hundred employees enjoyed the event, whose main attraction was a rich variety of ethnic foods and a celebration of Asian heritage at NIH. This is the 42nd year such a celebration has been held at NIH. Representatives from local restaurants such as Shanghai Cafe, Tandoori Nights, Ben & Jerry's and Matt's Kabobs introduced their cuisine for NIH employees.

APAO sponsored tables where guests could try Japanese origami, Chinese calligraphy and learn about the health benefits of tea. There were also vendors selling jewelry and other items. This year, representatives from other NIH groups supported the event, including the Employee Assistance Program, NIH Federal Credit Union, PHS APA Commissioned Corps, PHS scientist professional advisory committee, NIMHD, NIAMS and NIH R&W. Part of the proceeds from food and sales will be donated to the Children's Inn at NIH.



At left, employees lined up to enjoy lunch from Tandoori Nights.

PHOTOS: RUBY LEE



Architect Richard Banks designed the Rall Bldg. (l) to work with the environment, a quality that has kept the building fresh for more than three decades. At right, NIEHS Special Assistant for Community Engagement and Outreach John Schelp (l) joins (from l) Richard, Marilyn and Erik Banks on the balcony outside NIEHS director Dr. Linda Birnbaum's office, which offers a view of how the master plan for the campus has come to life.



The Rall Bldg.'s green and fit retrofit team included (from l) Debra Del Corral, Joseph Seufert III and Amanda Thompson. They helped cut overall construction costs by 30-40 percent by eliminating multiple project phases. Other efficiencies saved at least \$160,000. The project improved space utilization by eliminating passageways and optimizing layouts.

PHOTOS: STEVE MCCAIG

Architect Revisits NIEHS Campus He Helped Create More Than 30 Years Ago

More than three decades after the NIEHS campus was completed, lead design architect Richard Banks paid his first visit to learn how his brainchild has flourished over the years.

Over lunch in the NIEHS cafeteria recently, Banks described his concept for Bldg. 101, also known as the Rall Bldg. Banks emphasized the support he received from former NIEHS director Dr. David Rall.

"He was a great champion of the design of this building," Banks said. "He was behind it all the way."

According to Banks, it was an uphill struggle to retain several pioneering elements, unusual in government buildings at the time, such as the interstitial spaces between floors that allow access to utilities without disrupting work in the labs and offices.

"The mandate was flexibility, and our response was a systems building, modular in concept," he said. "We proved to them that it would be much more economical to do away with the corridors behind the labs and service them from above," Banks said. "They were very skeptical...[but] finally they came over to our side."

Among the innovations Banks introduced to the young institute were centralized glassware and media operations and mail distribution, all housed in a mall-like area. When completed, the Rall Bldg. was so far ahead of its time that location scouts for Woody Allen's science fiction parody *Sleeper* seriously considered it as a set for the film.

Banks is gratified to see how well his creation has aged. "For a building that's [almost] 40 years old, I am shocked by how good a condition it's in," he said of his progeny. "Usually, you don't find that in a government building."

Carrying forward the vision of a building that

works both for its occupants and its environment, the NIEHS green and fit retrofit team—which oversaw a recent renovation of part of the building—was named a 2014 HHS Green Champion. The team, led by Debra Del Corral and Amanda Thompson of the NIEHS Office of Management and Joseph Seufert III of the NIH Office of Research Facilities, won a Sustainable Design and Facilities Award.—Eddy Ball



Pancakes, Turkey Tails or Artist's Fungus?

"This is on a tree on the south side of the campus, on the walkway just outside the gate near Lot 41. I thought it was an extremely interesting fungus," said Richard W. Clark of NIAMS's Office of Science Policy, Planning and Communications. "Almost looks like pancakes! The closest I can come to identifying it is 'Artist's fungus' (*Ganoderma applanatum*)."

NIH landscape architect Lynn Mueller said, "They are often called 'turkey tails' and are indicative of interior heartwood rot or root rot. There are many species of this fungus. I'm more concerned about what their appearance means. We will perform an investigative sounding on the tree to determine its interior health."

PHOTO: RICHARD CLARK