

ABOVE • NEI intern makes finals of Intel science competition. See story on p. 7.

features

1
Sleep Appears to Serve as Brain's Clean-Up Time, Says Nedergaard

3
Good Health Is World's Wealth, Clayton Tells UN Forum

5
Greenberg To Give Chanock Lecture

12
Summit on Increasing Diversity in Science, Medicine

departments

Briefs	2
Digest	10
Milestones	11
Feedback	11

nih record

Welcome to the Glymphatic System

Nedergaard Explores Why We Need Sleep

By Rich McManus

We all know why that guy over there needs sleep—pew, did you get a whiff of him?—but Dr. Maiken Nedergaard thinks she knows why the rest of mankind needs sleep, and why without it, we die.

In a recent Wednesday Afternoon Lecture titled “The Nightlife of the Brain”—who can resist that?—she showed painstaking scientific evidence that the brain has its own public works system. Yes, a subdural network of utilities—okay, a sewer system—much like what undergirds New York and Washington (but perhaps more aromatic).

And the odd thing about it is that it has what you might call the discretion to function mainly while a person is asleep. That’s right, it goes to work when you lay down for a bit of kip. It’s like the housekeeping staff that descends on a midtown office building after hours.



Dr. Maiken Nedergaard at NIH

SEE NEDERGAARD, PAGE 6

Genomic Discoveries

Genetic Sequencing Paves Way Toward Preventing, Treating Disease

By Dana Talesnik

A mile-long park with intertwining sidewalks winds through the campus of the HudsonAlpha Institute for Biotechnology in Huntsville, Alabama. The double helix-shaped path is a fitting centerpiece for the research institute, flanked by biotech companies, which together strive to understand genomic pathways and make strides toward combating disease.



Dr. Richard Myers

With the potential of precision medicine—an emerging, targeted approach to treating disease by taking an individual’s genes into account—research institutes such as Hudson-

SEE SEQUENCING, PAGE 4

Be the ‘Better Getter-Upper’

Resilience Can Make a Difference, Says Olympian St. John

By Eric Bock

Being resilient can make a big difference. Leadership consultant Bonnie St. John stressed that point at a recent Deputy Director for Management Seminar in Masur Auditorium.



Bonnie St. John

Despite having her right leg amputated at age 5, St. John became the first African American to win Olympic or Paralympic medals in ski racing. She told of how she fell during her last race, at the 1984 Winter Paralympics in Innsbruck, Austria. Despite falling, she still won the silver medal for her

SEE ST. JOHN, PAGE 8



The NIH Record is published biweekly at Bethesda, MD by the Editorial Operations Branch, Office of Communications and Public Liaison, for the information of employees of the National Institutes of Health, Department of Health and Human Services. The content is reprintable without permission. Pictures may be available upon request. Use of funds for printing this periodical has been approved by the director of the Office of Management and Budget through September 30, 2015.

To receive alerts to our latest issue, send an email to listserv@list.nih.gov with the words "Subscribe NIHRECORD" in the message body.

NIH Record Office Bldg, 31, Rm. 5B41
Phone (301) 496-2125 Fax (301) 402-1485

Web address <http://nihrecord.nih.gov/>

Editor
Richard McManus
Rich.McManus@nih.gov

Associate Editor
Carla Garnett
Carla.Garnett@nih.gov

Staff Writers
Eric Bock
Eric.Bock@nih.gov

Dana Talesnik
Dana.Talesnik@nih.gov

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

NIH...Turning Discovery Into Health



10 Years of NIH News in Health

This month marks the 10-year anniversary of *NIH News in Health*, a monthly newsletter featuring accessible health information based on important current research results from NIH's 27 institutes and centers and their extramural grantees.

NIH News in Health is written at an 8th-grade reading level and is not copyrighted. Readers are encouraged to reprint the articles and illustrations in print or web publications. Each issue directly reaches more than 200,000 subscribers, who in turn share the expert-reviewed information with their friends, family and communities. Recipients include community health clinics, senior centers, libraries and nonprofit organizations. Stories are also reproduced in a variety of languages at the local community level.

Articles over the publication's 10-year history have ranged from the importance of healthy eating and physical activity to the microbiome, personalized medicine and the hazards of stress. "Our aim is to give people the knowledge and tools they need to improve their own health," says founding editor Dr. Harrison Wein.

"The stories show how NIH's wide-ranging research and expertise can directly affect our everyday lives," adds editor Vicki Contie. The newsletter is published by the NIH Office of Communications and Public Liaison. You can sign up to receive it at <http://newsinhealth.nih.gov/subscribe>. Contact the editors about sending it to communities that you work with.

Postbaccalaureate Poster Day Set, Apr. 30

Postbac Poster Day is scheduled for Thursday, Apr. 30 at the Natcher Conference Center from 10 a.m. to 3:30 p.m. This year, Dr. Audrey J. Murrell, associate dean and professor, Joseph M. Katz Graduate School of Business, University of Pittsburgh, will present the keynote address at noon. The keynote will be followed by presentation of the Postbac Distinguished Mentoring Award(s) to NIH investigators selected by the

postbacs. Poster Session I is from 10 a.m. to noon; Poster Session II runs from 1:30 to 3:30 p.m.

Poster Day provides an opportunity for postbacs to share research they have been conducting at NIH and at the same time develop their scientific communication and networking skills. Posters will be reviewed by teams composed of graduate students, postdocs and staff scientists/clinicians. Authors of the top 20 percent will receive a letter acknowledging their accomplishments.

Investigators, staff scientists and scientific administrators can make an important contribution to the event by visiting posters and engaging the authors in discussion. For more information, visit https://www.training.nih.gov/postbac_poster_day.



Berkeley's Doudna Describes CRISPR Science

One of the hottest current fields in science is CRISPR (clustered regularly interspaced short palindromic repeats)-Cas genome editing. One of the pioneers of the field, Dr. Jennifer Doudna of the University of California, Berkeley, recently described how the field emerged during the past decade. Her talk, "CRISPR-Cas genome surveillance: From basic biology to transformative technology"—the annual NIH Director's Margaret Pittman Lecture—can be seen at <http://videocast.nih.gov/summary.asp?Live=15743&bhpc=1>.

PHOTO: BILL BRANSON

Valentine To Give Roberts Lecture, Apr. 21

Dr. Hannah Valentine, NIH's chief officer for scientific workforce diversity, will give a talk in the 2015 Anita B. Roberts Lecture Series: Distinguished Women Scientists at NIH.

Her lecture, "Precision Medicine in Action: Applying Genomic Tools to Improve Patient Outcomes After Organ Transplantation," will be held on Tuesday, Apr. 21 at 1 p.m. in Lipsett Amphitheater, Bldg. 10. The series is sponsored by the NIH women scientist advisors committee and the Office of Research on Women's Health. It highlights outstanding research achievements of women scientists in the NIH Intramural Research Program.

Valentine is the first NIH chief officer for scientific workforce diversity and is also a senior scientist in the National Heart, Lung, and Blood Institute. She is internationally recognized for her clinical research program that continues to yield high-impact transformations in patient care. Her work focuses on implementing non-invasive approaches for the diagnosis of acute heart transplant rejection, an innovation that represented a major paradigm shift in the way heart transplant patients are managed.

In addition to leading a successful clinical research program, she is nationally recognized for her transformative approaches to diversity and is a recipient of the NIH Director's Pathfinder Award for diversity in the scientific workforce.

The seminar series is dedicated to the memory of Roberts, chief of NCI's Laboratory of Cell Regulation and Carcinogenesis from 1995 to 2006, honoring her role as an exceptional mentor and scientist. Prior to her death in May 2006, she spent 30 years at NIH performing pioneering work on transforming growth factor beta.

The lecture is open to all and will be followed by a question-and-answer session. Sign language interpreters will be provided upon request. Those who need reasonable accommodation to participate should contact Margaret McBurney at (301) 496-1921 and/or the Federal Relay, 1-800-877-8339, 5 days before the lecture.



Clayton at UN: 'Good Health Is Wealth for the World'

"Good health of women and men, and of girls and boys, is wealth for the world," said Dr. Janine Austin Clayton, NIH associate director for research on women's health, at the United Nations recently.

As keynote speaker at the inaugural World Women's Health and Development Forum, Clayton joined international health care leaders, UN representatives, scientists and activists to discuss how best to advance the health, wealth and empowerment of women worldwide. The UN department of economic and social affairs and the Royal Academy of Science International Trust organized the forum.



NIH's Dr. Janine Clayton (l) with Dr. Nisreen El-Hashemite, executive director of the Royal Academy of Science International Trust at the United Nations

PHOTO: ANNE RANCOURT

Citing the landmark Women's Health Initiative, which fundamentally changed how clinical care is delivered for women, Clayton argued that such research makes economic sense. According to a 2014 analysis published in the *Annals of Internal Medicine*, the WHI's clinical trial yielded a 140-fold return on its initial research investment over the past decade. That analysis also calculated that the WHI effort spared 75,000 women from heart disease and prevented 126,000 women from getting breast cancer.

Scientific research offers our best chance for improving the health and lives of women around the world, Clayton asserted, adding that more work needs to be done to understand the roles of sex and gender in health.

"Unfortunately, in 2015, we still know little about female biology and the influence of sex as a biological variable," she said. To date, animal studies have focused primarily on males; investigators studying cells in the laboratory have often not paid attention to the sex of the individual from which the cells were obtained.

This knowledge gap contributes to less effective care for women, Clayton added, noting that when a woman's health improves, the health of her family and community also advances. Empowering women and girls was one of the UN's eight Millennium Development Goals, a blueprint agreed to by all the world's countries and all of the world's leading development institutions. Currently, the UN is seeking input on the next generation of development goals. That was one reason for hosting this year's forum.

Clayton updated forum attendees about a policy shift in which NIH will ensure that preclinical researchers consider sex at the outset of their experiments. She recognized ongoing efforts in this arena, noting the World Health Organization's Strategy for Integrating Gender Analysis and Actions, which calls for mainstreaming a gender perspective at all levels, from research to legislation to policies and programs.

Collaboration across boundaries is critical for building this important foundation of knowledge "that provides hope for the day in which each global citizen—every male and female child, and every male and female adult—gets precisely the care they need for a healthy and productive life," she said.

For more information on NIH efforts to take sex into account in preclinical research, visit www.nih.gov/sexinscience.—Alison Davis and Anne Rancourt

SEQUENCING

CONTINUED FROM PAGE 1

Alpha are conducting important research with the help of NIH funding. Investigators are using new DNA sequencing technologies with the goal of treating patients with severe diseases caused by genetic variants.

Investigators at HudsonAlpha are conducting whole-genome sequencing as well as deeper, targeted sequencing, said Dr. Rick Myers, faculty investigator, director and president of HudsonAlpha Institute. He spoke at a recent NHGRI lecture in Lipsett Amphitheater. Lab data already has helped uncover genetic causes of more than 10 inherited diseases, including autism, ALS (amyotrophic lateral sclerosis), diabetes and bipolar disorder. Projects are also under way to delve



Each spring, runners traverse the 1-mile path along Genome Way in McMillian Park (Huntsville, AL) for the Double Helix Dash, a community event organized by the HudsonAlpha Institute for Biotechnology.

PHOTO: MARTY SELLERS

deeper into the genetic causes of cardiovascular disease and kidney cancer.

The institute's Genomic Services Laboratory operates more than a dozen high-performance sequencing instruments, Myers said, and recently acquired several Illumina X Ten systems—the latest, fastest and most powerful for whole-genome sequencing. Since its founding in 2009, HudsonAlpha has processed more than 80,000 samples and collaborated on more than 1,800 projects with hundreds of labs worldwide.

Investigators have made promising advances in their study of ALS, a progressive disease characterized by muscle atrophy. Part of a 2-year collaborative project, the study is examining 3,000 ALS cases through custom capture and whole-genome sequencing. So far, they've found at least 9 familial forms of ALS and several genes of interest, including a gene involved in loss of function mutations that plays a role in inflammation and autophagy (the breakdown, discarding and recycling of cells). And biotech companies are interested in these genes as targets. Myers said, "The hope is the drugs may even work for multiple diseases."

Sequencing projects are also under way for cancer patients. From findings of gene fusions in breast cancer, one company is manufacturing antibodies to recognize these fusions and develop a cellular toxin to kill the cancerous cells. Another promising development is a biochemical process called DNA methylation that's helping investigators search for biomarkers to predict risk and recurrence probability for aggressive forms of cancer. "The remarkable thing is [that] the specificity and sensitivity of any 3 or 4 of these biomarkers is amazing," said Myers. The hope, he said, is to test DNA in urine and blood to improve routine screening for earlier detection and better treatment.

Another focus of HudsonAlpha research is childhood genetic disorders, often characterized by intellectual disability, developmental delay, heart defects, cra-

niofacial abnormalities and/or seizures. Some 1.5-3 percent of children worldwide are born with one or more of these anomalies.

"These are significant public health problems," said Myers. "We believe that most of these are genetic and that's starting to pan out, a function of doing these kinds of projects."

In one ongoing pediatric project, part of CSER (Clinical Sequencing Exploratory Research) in conjunction with NHGRI, investigators are recruiting and conducting whole-genome sequencing on 450 families. Since we all carry mutations, said Myers, it takes time to discern if there's a single gene for a disorder. He cited a curious example of atypical Rett syndrome, where they found two unrelated kids who had different mutations yet neither child had seizures, a common symptom of the disease. In analyzing the results, Myers said, it's an arduous task figuring out whether variants are pathogenic. "As soon as you get 2 or 3 or 4 mutations with a similar phenotype," he said, "you'll probably know that you've got it."

A frustration with patients of any age, said Myers, is the needless anguish caused by undiagnosed diseases. Patients might see many doctors and go through years of futile, invasive testing at great personal expense only to get an inaccurate diagnosis or none at all.

That's why identifying root genetic causes is important. "You can't do anything if you don't know the cause," said Myers. Some conditions may appear similar but we can't be sure without knowing the phenotype, and there are many genes and potentially many, maybe thousands, of causes. "I learned this from my first foray into human genetics: When people don't know, they blame themselves, which is horrible," said Myers. "If you can figure out the cause, [it can make a huge difference] in the relatively few cases where you can actually do something about it."

While working on many genomic projects, HudsonAlpha also seeks to educate and inspire future generations of scientists. The institute sponsors "cradle-to-grave education," said Myers; every kid across Alabama gets free lessons. In addition to courses, he said, their publications highlight "exciting happenings in genomics written in everyday language where everybody can understand it. This is something we put enormous effort into and we think it's as important, if not more important, than our research." 📍



Greenberg To Give NIAID Chanock Lecture, Apr. 28

Dr. Harry Greenberg, senior associate dean for research and Joseph D. Grant professor of medicine and microbiology and immunology at Stanford University School of Medicine, will present the annual NIAID

Robert M. Chanock Memorial Lecture. His talk, "Innate and Acquired Immunity to Rotavirus: New Mechanisms and Old Tricks," will take place on Tuesday, Apr. 28 at 9 a.m. in the Bldg. 50 1st floor conference room. The lecture honors Chanock, who served as chief of the NIAID Laboratory of Infectious Diseases for more than three decades.

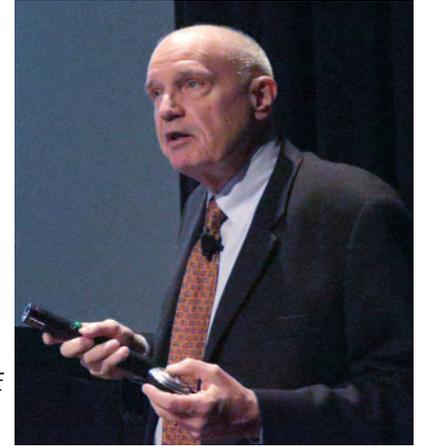
Greenberg will discuss rotaviruses, a genus of viruses that cause severe and often fatal diarrhea in children, especially in poor countries. Rotaviruses are regulated by a variety of innate and acquired host immune responses. While they are generally good at evading the host's innate immune response, rotaviruses have been less successful in circumventing the host's acquired immune system. A variety of studies have shown that a single natural rotavirus infection or vaccination with a single type of rotavirus will protect against many types of subsequent rotavirus-associated diarrheal disease, especially severe disease. To track where this immunity develops, Greenberg's group isolated rotavirus-specific B cells and used gene sequencing to map the possible evolution of rotavirus-specific antibodies. Their results identified specific targets that—with further characterization—will provide the basis for designing more effective future vaccines.

Greenberg was a co-inventor of the first effective rotavirus vaccine; his studies have helped define the nature of rotavirus immunity and pathogenesis. He received his B.A. from Dartmouth College and his M.D. from Columbia College of Physicians and Surgeons. He completed residency training in internal medicine at Bellevue Hospital in New York and a fellowship in gastroenterology at Stanford University School of Medicine. He served as a medical officer in NIAID's Laboratory of Infectious Diseases for 9 years before joining the Stanford faculty as an associate professor of medicine and microbiology and immunology. He also works as director of Spectrum, the Stanford Center for Clinical and Translational Research and Education.

Atkinson Honored as NIH Distinguished Scholar, Educator

By Janet Hulstrand

Dr. John P. Atkinson, a renowned researcher in autoimmunity and chronic inflammation, is this year's Distinguished Clinical Research Scholar and Educator in Residence, the third to be so honored. Atkinson, a Samuel B. Grant professor of medicine, professor of molecular microbiology and chief of the division of rheumatology at Washington University School of Medicine in St. Louis, was the speaker at Clinical Center Grand Rounds recently.



His research focuses on complement regulatory proteins, a system of proteins abundantly present in blood that help to destroy disease-causing bacteria and viruses. His clinical activities center on patients with immune dysfunction including lupus, immunodeficiencies and rare inflammatory disorders. His lab's recent clinical and translation activities have focused on identifying genetic mutations in complement inhibitors predisposing to human diseases.

He spoke about the effects of such mutations predisposing to atypical hemolytic uremic syndrome and age-related macular degeneration. One interesting aspect of this work is the implication that immune modifiers with a strong genetic basis, probably designed to protect babies from infection, have a tendency to "backfire" in old age. By this he means that evolutionarily driven alterations that protect, for example, against a lethal strep or plague bacillus infection in childhood may cause trouble (too much inflammation) when our immune systems have to deal with biologic debris, such as in age-related macular degeneration.

Atkinson has a long association with NIH. In the 1970s, he was a clinical associate under Shelly Wolfe, a doctor who greatly influenced immunology and infectious diseases research within the National Institute of Allergy and Infectious Diseases' Laboratory of Clinical Investigation. Atkinson also spent years studying the workings of the complement system. He has served as chairman of the Clinical Center's board of scientific counselors, on the National Advisory Council for the National Institute of Arthritis and Musculoskeletal and Skin Diseases and as an external advisor for the NIH Undiagnosed Diseases Program. He serves on the National Human Genome Research Institute board of scientific counselors and will become chairman of the board in the fall.

Atkinson has trained more than 70 pre-doctoral students and postdoctoral fellows, many of whom have gone on to distinguished careers in academia, government and the biotechnology and pharmaceutical industries.

"NIH was and is a great place to train as a physician-scientist," he said. "I feel like NIH is my second home. I was so fortunate to be exposed to and learn how to perform clinical investigation. I still have a hard time believing that someone would actually pay me to do exciting detective work on the etiology, pathogenesis and treatment of human disease in such a great place."

In addition to giving Grand Rounds, Atkinson met with medical students, fellows in a variety of disciplines and investigators from a number of institutes during his 2-day residence. The Distinguished Clinical Research Scholar and Educator in Residence is supported by funds the Clinical Center received as part of the Lasker-Bloomberg Public Service Award in 2011.

View the lecture at <http://go.usa.gov/3cUtw>.



NEDERGAARD

CONTINUED FROM PAGE 1

Above:

The photo of the brain that seems to hover over Nedergaard was part of her presentation on a waste-removal system in the brain known as the glymphatic system.

PHOTOS: BILL BRANSON

Nedergaard, who is Frank P. Smith professor of neurosurgery and co-director of the Center for Translational Neuromedicine at the University of Rochester Medical Center, has long been fascinated by glia, a unique cell type found only in the brain.

In her view, the brain may indeed be a nest of connections, but it is not a computer. It's an organ, just like lungs and kidneys. The same things that make lungs and kidneys happy—exercise, food and rest—make brains happy.

Nedergaard, who is not trained in sleep studies, asked a simple question: What keeps a brain healthy? “A nice night of sleep is best to keep it in shape,” she said. But more than that, sleep is an essential phenomenon. Flies, rats and humans all die if their brains don't experience sleep. There is a part of the brain—the locus ceruleus—in which dendrites die if sleep is withheld.

She reviewed a number of theories about what makes sleep a biological imperative, including benefits to memory, the immune system and the sheer preservation of human energy, given that a sleeping person's metabolism slows by 15 percent vs. waking hours.

Sleep's importance is further underscored by circadian rhythm, which keeps us in sync with the day/night cycle and is regulated by a sophisticated network of clock genes. Work late a few evenings and you begin to experience “sleep pressure,” which builds up in no other organ in the body except brain. “What drives that?” Nedergaard wondered.

She and her colleagues noted that the brain and spinal cord lack a lymphatic system, which plays a key role in the immune system. “Why does the brain not have it?” they asked, especially when brain tissue has 10 times the energy demand of other human tissues and would likely need a way to dispose of excess proteins and fluids.

Nedergaard and her team realized that a number of neurological disorders—including Alzheimer's disease and other dementias—are characterized by an accumulation of proteins. Could such illnesses boil down to something like a sewage backup?

The scientists found that cerebrospinal fluid (CSF) can act as a sink for waste—the brain can actually export molecules to the liver. Studies in rodents showed that glia in the brain are the headwaters of tiny rivers that end up in the lymph nodes of the neck. This partnership—a macroscopic pathway in the central nervous system—they dubbed “the glymphatic system.” It facilitates the clearance of interstitial waste products from neuronal metabolism, she said.

They discovered a phenomenon they called CSF pulsation—the brain, which gets a disproportionate amount of the body's blood supply (Nedergaard said the brain pumps more fluid than the kidney)—actually throbs like a beating heart.

According to her lecture summary, “The glymphatic clearance of macromolecules is driven by CSF that flows along para-arterial spaces and through the brain parenchyma via support from astroglial aquaporin-4 water channels. The glymphatic circulation constitutes a complete anatomical pathway: para-arterial CSF exchanges with the interstitial fluid, solutes collect along para-venous spaces and then drain into the vessels of the lymphatic system for ultimate excretion from the kidney or degradation in the liver.

“The peri-vascular space is very unique,” said Nedergaard, describing a loose fibrous matrix around such vessels as pial arteries that act as a highway for fluid flow. She credited NINR director Dr. Patricia Grady with making a key observation about this system, years ago, in a paper on para-vascular fluid circulation in the mammalian central nervous system. “It created a lot of excitement in the field,” said Nedergaard.

The recent paper “Go With the Flow,” published by Nedergaard's team in *Science* in 2013 and named one of its top 10 reports that year, describes the intricate micro-plumbing that clears the brain of debris such as amyloid.

Further work in mice has demonstrated that,

while the glymphatic system is always functioning, it is much more active when the animal is asleep. The difference “is like turning a faucet on and off,” Nedergaard reported.

Somehow—the work is still ongoing—the volume of interstitial space in mammalian brain expands during sleep. The pipes fly open. Deprive an animal of sleep and the diffusion of fluid is reduced, with potentially drastic consequences.

Nedergaard noted that her team’s work has immediate implications for clinical care of patients with traumatic brain injury.

“Stop waking them up every 10 minutes to take vital signs,” she counseled. That sleep they are getting is actually healing them.

Also, TBI patients often have portions of their skulls removed temporarily, to relieve swelling. Nedergaard says it’s important to patch these holes up quickly because it restores convective flow of CSF. “Patients get better faster,” she said.

Nedergaard’s talk can be viewed at <http://videocast.nih.gov/summary.asp?Live=15718&bhcp=1>.

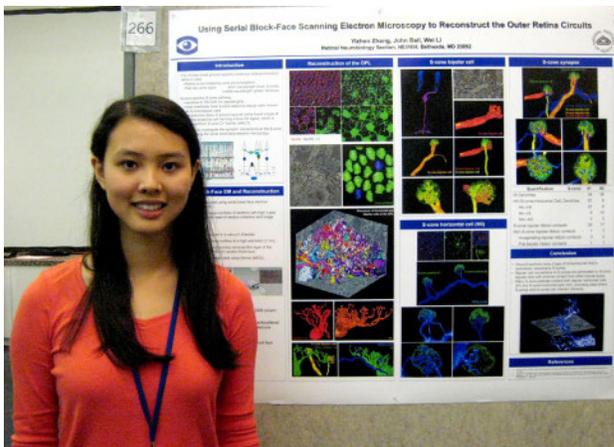
R&W’s Schools Honored at Retirement

Randy Schools was honored Mar. 12 at the Hyatt Regency Bethesda for his 38 years of leadership at the NIH Recreation & Welfare Association. Well-wishers included Ike Leggett (top photo), Montgomery County executive, NIH colleagues and community leaders with whom Schools has deep ties.

Greetings from Maryland Gov. Lawrence Hogan were read and attendees could view citations honoring Schools from Sens. Barbara Mikulski and Benjamin Cardin of Maryland, Rep. Chris Van Hollen, the Greater Bethesda-Chevy Chase Chamber of Commerce and the Bethesda-Chevy Chase Rescue Squad. Guests enjoyed dinner, remarks and a commemorative cake served by Schools and his wife, Barbara (above).



PHOTOS: BILL BRANSON



Yizhen Zhang, a senior at Richard Montgomery High School in Rockville and 2014 summer intern at NEI, is one of 40 finalists in the Intel Science Talent Search this year. She presented her work at a poster session at the National Geographic Society in Washington, D.C.

NEI Intern Makes Intel Science Finals

Yizhen Zhang, a senior at Richard Montgomery High School in Rockville, is one of 40 finalists in the Intel Science Talent Search this year. Her 12-week project while a summer 2014 intern with Dr. Wei Li in NEI’s retinal neurophysiology section drew the attention of judges from the Society for Science and the Public, which runs the competition for high school seniors with sponsorship from Intel Corp. Zhang presented her work at a poster session during a weeklong conference in March at the National Geographic Society in Washington, D.C., and competed for up to \$150,000 in awards.

Her project, with technical assistance from Dr. John Ball, a postdoctoral fellow in the lab, involved short wavelength sensitive cone photoreceptors (also known as the blue or S-cones). These cones are essential in allowing mammals to see blue, which is important for circadian rhythms and eye development, as well as cognitive functions.

Zhang used the 13-lined ground squirrel, also known as the striped gopher, to create the first connectome, or neural wiring map, of the S-cone. By applying serial block-face scanning electron microscopy to reconstruct the cone terminals, she gained insight into the retinal circuits used for color processing. This line of work will provide knowledge of how the retina encodes color information. It could also help lead to interventions for certain forms of color blindness, which has been a motivation for Zhang ever since she met a group of colorblind students.

In addition to becoming an Intel finalist, Zhang was also a semi-finalist in the Siemens Competition in Math, Science and Technology. “Yizhen wanted to participate in both competitions because she liked writing up her work,” said Li. “This isn’t seen often in students.” What stood out for Li was Zhang’s intensity and focus. “She drove the project and process, even driving me,” he said.

Zhang didn’t think she would go far in the Intel competition. “It really surprised me when I got the call saying I was a finalist,” she said. She credits Li and Ball’s support of her work with her success in the competition. She plans to continue in ophthalmic research in college with the hope of eventually getting her Ph.D. in neurobiology.—Cesar Perez-Gonzalez

ST. JOHN

CONTINUED FROM PAGE 1

overall performance. After the race, she heard that the gold medal winner also fell down.

“I could’ve won gold if I got up a little faster,” she said. “It’s so important to think about resilience even when you’re at the top of the game. Sometimes the person who wins gold is just the better getter-upper.”

St. John identified two types of resilience: “macro” and “micro.” Macro-resilience refers to lifestyle choices that help people become more resilient over a few weeks or months. Examples include eating a balanced diet, drinking enough water, exercising regularly and getting enough sleep.

“Micro-resilience is the ability to do better hour-by-hour, every day,” she said. “The payoff of micro-resilience is you’re going to do better today.”

To illustrate the difference between the two, she spoke about the need to drink water during a time of stress.

“Micro-resilience is the ability to do better hour-by-hour, every day. The payoff of micro-resilience is you’re going to do better today.”

From a macro-resilience perspective, if someone doesn’t drink any water while working on a stressful project, he or she will be alright, provided the person drinks more water later in the day, after the stressful time has passed.

From a micro-resilience perspective, however, drinking water during the stressful time is precisely when it’s needed most. A person’s brain contains a higher percentage of water than the rest of the body, so the brain dehydrates before people realize they’re thirsty. So, deciding when to drink water is important from the micro perspective.

St. John said that human beings evolved as hunter-gatherers over millions of years. Based on their history, she said, people alive today have inherited the genes of the “worriers, the people who reacted.” That means, she added, that people tend to spiral into the negative, which can trigger tunnel vision.

These reactions aren’t helpful in today’s fast-paced world. St. John said people need to think creatively, work together and look ahead during



To improve productivity, St. John said, employees can take breaks during the day to stretch, exercise or go for a walk.

PHOTOS: ERNIE BRANSON

stressful times, rather than reacting to events as they happen.

“The good news is we can rewire,” St. John said. “We like to think of it as an upgrade to the human operating system.”

When people first become stressed, St. John said a few calming strategies are useful. First, they can describe their feelings.

“If you can say it, you can look at it and you can be an observer, not just be one with it,” she said.

One can also practice deep-breathing exercises or muscle-relaxation techniques. She added that certain smells, like cinnamon or vanilla, can calm a person down.

Next, St. John said people need to understand the limits of their brain.

“Our prefrontal cortex is really small. It’s a late add-on in the evolutionary process,” she said. It is believed to be involved in higher-order thinking. “When we respect that it’s small, we can actually use our brain better and more effectively.”

To improve productivity, she said, employees can take breaks during the day to stretch, exercise or walk.

St. John advised workers to avoid multi-tasking because it degrades quality, accuracy and creativity. Instead, they should set aside time during the day to accomplish one task. She also recommended that employees make fewer decisions during the day.

“The more decisions you make, the more tired you get,” she said. To combat what St. John called “decision fatigue,” employees can make important choices early in the day. Checklists can also limit how many decisions are made in a day.

She also said it’s important to cultivate a positive outlook through regular positivity exercises.

“There are so many situations where we tend to spiral into the negative, but it would be helpful to stay positive,” she noted.

She suggested supervisors begin meetings by asking employees to say something good that happened during the past week. She also said people can put together a “joy kit” of things that make them happy, to serve as reminders of happier times. These might include a bottle of sand from a beach vacation or a recording of a child’s laughter.

St. John also advised people to eat regularly to keep their energy up and to drink water to stay hydrated.

Finally, she said it’s important to stay in touch with one’s purpose, which she referred to as one’s “values plus goals.” It’s easy to lose track of purpose because of day-to-day details. Some people put reminders on their car’s dashboard, in their office or on their computer screensavers to remind them of what’s important to them and why they do what they do.

Although these strategies won’t slow down the world, practicing micro-resilience can speed up recovery time, she noted.

Focusing on such smaller, incremental “resets” throughout the day offers immediate and intentional activities that combat the natural, physiological, hard-wired tendencies that allow people to be hijacked by the stress of the work day, she concluded. 🌀

CÓMO VIVIR CON LUPUS

Información básica de salud para usted y su familia



NIAMS Takes On ‘Language Access’

The Affordable Care Act has made it possible for millions of people to attain affordable health coverage. However, people with limited English proficiency face a daunting challenge upon entering the health care system—language barriers. According to recent Census estimates, nearly 20 percent of the U.S. population, about 55 million people, speak a language other than English at home.

NIH has addressed this challenge by establishing the NIH Language Access Plan, a comprehensive strategy being implemented across the agency to help people with limited English proficiency access NIH programs and activities. “The Language Access Plan, which is a critical component of NIH’s overall diversity and inclusion efforts, helps ensure that individuals, regardless of their language ability, can access important health information and participate in clinical trials,” said Debra Chew, director of the NIH Office of Equity, Diversity and Inclusion.

NIAMS is one of several ICs at the forefront of making health information more accessible to people from underserved communities. “Many diseases in our scientific portfolio, including lupus, arthritis and osteoporosis, have profoundly negative effects in minority communities in terms of prevalence and poor health outcomes,” said Dr. Stephen Katz, NIAMS director. “As our country becomes increasingly diverse, it is our responsibility to make sure quality health information is accessible to all people, no matter what language they speak.”

As part of its National Multicultural Outreach Initiative, NIAMS has expanded its suite of health information products to include publications in Spanish, Chinese, Vietnamese and Korean. Among the institute’s most popular publications is its *A Year of Health* planner series, which is tailored to four multicultural audiences—African Americans; Hispanics/Latinos; Asian Americans and Pacific Islanders; and American Indians, Alaska Natives and Native Hawaiians. Now in the third year of production, the planners continue to be well-received by communities nationwide not just for their practicality, but also for their cultural relevance. According to one health care provider, “Our clinic is always on the lookout for tools to help support our patients with complex health needs. We appreciate the bilingual and culturally specific [planners], as they are most appropriate for the patients we serve.” The bilingual health planner recently received a Gold Award from the Health Information Resource Center, a national clearinghouse for consumer health professionals who work in health education fields. NIAMS is one of three NIH institutes that received recognition in its National Health Information Awards Program.

Recognizing that social media is fast becoming the information platform of choice for many people, NIAMS regularly tweets in both English and Spanish. Recently, NIAMS coordinated a bilingual English/Spanish Twitter chat focused on lupus, an autoimmune disease that disproportionately affects Hispanic women.

The NIH Language Access Plan reinforces NIAMS’ steadfast commitment to ensuring that everyone in the United States has the same opportunity to live healthy, productive lives. “We are proud that NIH continues to be a leader in these efforts—within HHS and among federal agencies. NIAMS is a key partner and model in this work,” said Chew.—Mimi Lising

Strengthening the Immune System's Fight Against Brain Cancer

When cancer strikes, it may be possible for patients to fight back with their own defenses, using a strategy known as immunotherapy. According to a new study published in *Nature*, researchers have found a way to enhance

the effects of this therapeutic approach in glioblastoma, a deadly type of brain cancer, and possibly improve patient outcomes. The research was funded by NINDS and NCI.

"The promise of dendritic cell-based therapy and other immunotherapies for brain cancer has been upheld for some time, but an important implication of this work is a demonstrated capacity to significantly improve the clinical impact of immunotherapy for patients with this very difficult disease," said Dr. Duane Mitchell,

director of the Brain Tumor Immunotherapy Program at the University of Florida and co-lead author of the study.

Dendritic cells are specialized immune cells that normally capture microorganisms and then migrate to the lymph nodes to prepare other immune players, such as T cells, to fight off the invaders.

Dendritic cells have been used for immunotherapy to target a variety of tumor types, including those that affect the brain. These cells are taken from the patient, engineered to express antigens from the tumor to create a vaccine and then injected back into the patient. Once in the patient, the engineered dendritic cells activate T cells, which can fight the tumor and also prevent it from coming back, via an immune memory response.

For Most Children with HIV and Low Immune Cell Count, Cells Rebound After Treatment

Most children with HIV who have low levels of a key immune cell eventually recover levels of this cell after beginning treatment, according to a study by researchers funded by NIH.

Failure of CD4+ T cells, a major target of HIV, to rebound after the virus has been suppressed

with medication occurs in about 15 percent of adult patients and is associated with serious, life-threatening illnesses. The researchers conducted the current study to find out to what extent children who were infected with HIV around the time of birth might be at risk for this condition and whether this failure carried with it a major risk for serious infection.

"The good news is that this condition occurs only infrequently in young children with HIV," said study author Rohan Hazra of NICHD, which provided much of the funding for the study. "The comparatively few children whose CD4+ cells failed to rebound did not appear to be at any greater risk for serious infection than children with higher CD4+ counts."

He added that the findings do not appear to change treatment recommendations for children with HIV, which include antiretroviral drugs to suppress the virus and periodic follow-up examinations to detect the first signs of any serious infections.

The findings were published online in *AIDS* and the study was conducted by a team of researchers at several institutions in the United States and Brazil.

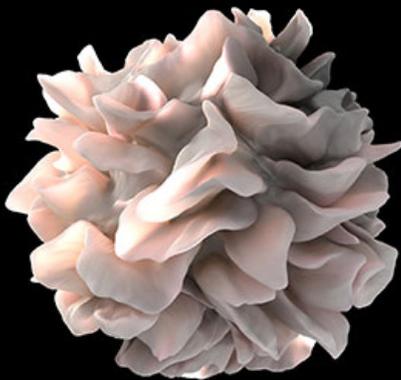
NIH-Funded Scientists Identify Brain Site for Stress Role in Binge Alcohol Drinking

New research shows how elements of the brain's stress and reward pathways can interact to suppress binge alcohol drinking. The finding, online in *Nature Neuroscience*, suggests potential strategies for treating and preventing alcohol use problems.

"This study is an important contribution to our knowledge of the neurobiology of alcohol-use disorders and could open new avenues for medication development," said Dr. George Koob, director of NIAAA, the primary sponsor of the research. NIDDK also provided support for the study.

Binge alcohol drinking contributes to myriad acute and chronic public health problems and accounts for an estimated three-quarters of the total economic cost of alcohol misuse. Accumulating evidence indicates that binge drinking by adolescents and college students contributes to alcohol dependence and anxiety disorders.

Previous studies have shown that brain signaling by a protein known as corticotropin-releasing factor (CRF) increases anxiety. CRF activity also increases during binge alcohol drinking. In contrast, a brain protein called neuropeptide Y is known to reduce binge drinking and anxiety. However, how and where these two opposing systems interact in the brain is unknown.



An artist's representation of the surface of a human dendritic cell. Engineered dendritic cells can fight tumors.

IMAGE: NCI

m

milestones



Dr. Carrie Wolinetz

Wolinetz Heads Science Policy Office

Dr. Carrie Wolinetz has been named new NIH associate director for science policy. She most recently served as deputy vice president for federal relations at the Association of American Universities. Her primary responsibility was to coordinate advocacy on funding and policy issues relating to NIH and biomedical research.

Outside of AAU, Wolinetz served as president of United for Medical Research, a coalition of universities, patient groups and private sector companies advocating for sustainable funding for NIH. In addition, she was an adjunct assistant professor at Georgetown University in the School of Foreign Service's program on science, technology & international affairs as well as past chair of the advocacy committee for the Association for Women in Science.

Wolinetz has a B.S. in animal science from Cornell University and received her Ph.D. in animal science from Pennsylvania State University, where her area of research was reproductive physiology.

Prior to joining AAU, Wolinetz was director of scientific affairs and public relations at the Federation of American Societies for Experimental Biology, where she worked on a portfolio of issues that included federal funding of research, the use of animals in research, cloning and stem cells and biosecurity.

f

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: Can we get an update on the deer management program? I am a fan of the deer. In the Dec. 5, 2014, article, the *Record* reported that there were about 40 deer on campus, but the tag numbers on the deer go up to at least 89. Why is that? Also, why are some wearing heavy looking neck rings?

Response from the Office of Research Services: During December 2014, 24 deer were spayed. The ear tags started at number 77 and went up to 99, then individually, numbers 30 and 35 were also used. The neck ring is a radio collar used to track the matriarch of the matrilineal line. This tracking will be particularly useful when the wildlife biologist returns this fall to count and assess the herd.

Feedback: The cafeteria in the Natcher Bldg. is too small and understaffed to handle the regularly occurring surges of people for conferences. Adding to the overflow, the seating area is smaller because of an added wall. The routine inability of this space to seat staff and visitors is inhospitable to visitors to our campus and contributes to an unfriendly workplace for colleagues who wish to lunch together. Perhaps conferences can be required to set up seating in the atrium or lobby to accommodate attendees who will certainly want to network over lunch.

Response from ORS: Thank you for your question. The Office of Research Services is aware of the issues in the Bldg. 45 cafeteria when there are largely attended conferences. In 2012, NIH decided, due to budget reductions, to reduce the size of the Natcher cafeteria and associated seating area, which would result in lowered rent costs. During normal daily operations, the size of both the cafeteria and the seating area are appropriate for the customer base. However, we are clearly stretched to more than capacity during largely attended events.

The cafeteria operator, Eurest, and our events management staff have been partnering to ensure that we are prepared for large events. Once construction is completed in the north end of the space, we will work with the NIH fire marshal to re-evaluate the number and configuration of tables and chairs permitted in the seating area. In addition, we have ordered several new café style tables and chairs to be placed in the atrium area to provide additional seating. The ORS Events Management Branch will also monitor future large events and require reservation of extra tables and chairs directly in the conference areas to provide additional seating for attendees.

We hope that these efforts will enhance the cafeteria experience and make it more comfortable for all.

Feedback: Three of the four elevators in MLP-8 are non-functioning. When will they be back in working order? It's only a matter of time [before the] fourth one goes out from overuse!

Response from the Office of Research Facilities: Elevators 1 and 2 in MLP-8 have been out of service since May 2014. Elevator 3 was shut down in January and was determined to need extensive repairs. The Office of Research Facilities elevator repair team has done everything possible to repair these elevators, including short-term repairs, to get the elevators back in service. However, all 4 elevators eventually need a complete modernization/overhaul for continued safe use and operation. Funding has been approved to replace one of the three out-of-service elevators; work towards this end will begin later this spring.

We apologize for the delay and are making every effort to complete this major repair project as quickly as possible to restore additional, safe elevator service in MLP-8.

In Search of Moonshot

Summit Focuses on Strategies to Increase Diversity in Medicine, Research

By Gerda Gallop-Goodman

The National Hispanic Medical Association, in partnership with the National Institute on Minority Health and Health Disparities, recently hosted a Consensus Summit on Building Diversity in Medicine and Research. A diverse group of 75 thought leaders gathered to share lessons learned, best practices and strategies and recommendations for enhancing workforce diversity in medicine and biomedical and behavioral research.

“This is an invitational meeting to bring together the best and brightest in medicine and research to determine ways to build pipelines and pathways for the next generation,” said Dr. Elena Rios, NHMA president and CEO. “We know how important it is to start now.”

In welcoming remarks, Dr. Lawrence Tabak, NIH principal deputy director, said, “Meetings like this are so crucial because we get to hear from those in the trenches, doing what needs to be done. You can help us think through how we can generalize these approaches and success stories.”

“It’s time for big ideas,” said Dr. Yvonne Maddox, NIMHD acting director. “Let’s make today a big moment. We have to think differently about how to address research workforce diversity. We need deans, department chairs and faculty at medical schools involved in changing policies on how they accept students and select administrative staff.”

Dr. Yvonne “Bonnie” Maldonado, senior associate dean for faculty development and diversity at Stanford University School of Medicine, encouraged participants to look for the moonshot—the big ideas and innovations—to engage inclusion, awareness and empowerment.

Featured speaker Dr. Hannah Valantine, NIH chief officer for scientific workforce diversity, discussed NIH’s new integrated strategy for expanding diversity in biomedical research careers. Approaches include establishment of national hubs for innovation in scientific workforce diversity; a renewed commitment to ensuring fairness in peer review; testing and evaluating evidence-based programs to diversify the NIH Intramural Research Program; and grants through the NIH Common Fund’s Enhancing the Diversity of the NIH-Funded Workforce program.



NIMHD acting director Dr. Yvonne Maddox (third from r) and National Hispanic Medical Association president and CEO Dr. Elena Rios (r) are shown at the summit with panelists (from l) Dr. Freeman Hrabowski, III, president, University of Maryland, Baltimore County; Dr. Monica Ramirez Basco, assistant director for neuroscience, mental health and broadening participation, Office of Science and Technology Policy; Dr. Ronald Copeland, senior vice president, national diversity strategy and policy and chief diversity officer, Kaiser Permanente; Dr. Wayne Frederick, president, Howard University; and Dr. Marc Nivet, chief diversity officer, Association of American Medical Colleges.

PHOTO: GENEVIEVE BLOOMER

“We need to be cognizant of why we need diversity and the nature of the problem,” she said. “Diversity is essential for good science. There are a number of risks we face that lack of diversity causes. We lose trust. Increased diversity leads to more committed scientists.”

Dr. Monica Ramirez Basco of the Office of Science and Technology Policy emphasized President Obama’s support of programs to enhance science, technology, engineering and mathematics efforts such as the Department of Energy’s \$25 million grant to support cybersecurity education at Historically Black Colleges and Universities.

Rather than creating a series of new initiatives, Dr. Ronald Copeland of Kaiser Permanente urged participants to consider an integrated approach to diversifying the medical and research workforce. “Value is created through integration, not fragmentation,” he said. “We need to harness the power of integration to bring things to scale, which involves tracking, infrastructure and measurable results over time and requires stakeholder engagement.”

Many students aspiring to careers in science and medicine drop out or change majors within the first 2 years of their studies when they become overwhelmed by the rigorous coursework, said Dr. Freeman Hrabowski, III, president of the University of Maryland, Baltimore County. “We need to rethink the first 2 years of a student’s career—change the structure of the classroom—and connect researchers to students at this critical point where they are deciding whether to stick with the challenge of scientific study or not,” he said.

Dr. Wayne Frederick, president of Howard University, called for more women and people of color on search committees and in leadership positions in academia, as well as increased financial assistance for students, such as Pell grants, and incentives for them to graduate on time. “We need to take away barriers that prevent students from succeeding,” he said.

NHMA will issue a summary report with recommendations from the meeting on the role of institutional leadership in building a diverse workforce in medicine and research and best practices in recruiting and sustaining diversity in biomedical and behavioral research and medicine. 🗎