NIH

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Barabino Sorts Out Mechanics of Sickle Cell Disease

BY RICH MCMANUS

Traffic jams are bad enough-remember the mass campus exit during Jan. 7's snow?-but what if they occurred in blood vessels throughout the organs of your body, from the eyes, to the liver, to the gall bladder, on down?

That is what sickle cell crisis inflicts on the millions of people worldwide who have sickle cell disease (SCD), including some 100,000 Americans, said Dr. Gilda Barabino, dean of engineering at the City College of New York, at a Jan. 28 talk in the Wednesday Afternoon Lecture Series.

SCD is a painful disease caused by a single



Dr. Gilda Barabino accepts honorary plaque from NIH principal deputy director Dr. Lawrence Tabak, who introduced her lecture. "It's not often that one can introduce a WALS lecturer who is a dean at their alma mater [City College of New York]," he said.

PHOTO: DR. MARIE A. BERNARD

amino acid that has gone awry and typically results in 30 years less life expectancy for those who have it, said Barabino. Cases of SCD are predicted to rise by 30 percent between 2010 and 2050, she added.

Normal red blood cells are like the fittest person at your gym, the one who is endlessly strong and flexible.

"The red blood cell is a marvel in both structure and function," said Barabino, who directs CCNY's Laboratory on Vascular and Orthopedic Tissue Engineering Research. "It has a bi-concave discoidal shape that permits the membrane to deform while maintaining a constant surface area without stretching. Its flexible dumbbell shape allows it to pass through vessels with a diameter half the size of the red blood cell itself."

But in SCD, red blood cells become deformed in low-oxygen conditions and adopt a sickle shape, their once-flexible

SEE SICKLE CELL, PAGE 4

Puppies provide therapy for doctors as well as patients. See story, p. 12

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Potential Treatment Found for Alcoholic Liver Disease

BY ERIC BOCK

An anti-inflammatory called hyaluronic acid 35 (HA 35) might one day protect



Keller Honorary Lecture in Lipsett Amphitheater on Jan. 28. "We're in the planning stage

patients from the

complications of

holic liver disease.

moderate alco-

said Dr. Laura

Nagy at NIAAA's

24th annual Mark

pilot clinical trial, to see whether providing HA 35 to healthy adults before a single alcoholic drink can protect the gut," said

NEW NEUROTECHNOLOGIES

Shanechi Explores How to Decode Mood

BY DANA TALESNIK

Sometimes it seems almost unpredictable. Our mood is often affected by many



Dr. Maryam Shanechi

conditions and variables. Could it really be possible to predict and control our mental state?

Such a prospect could bring relief to the many who suffer from neuropsychiatric disorders, including the millions

of people in the United States who have treatment-resistant major depression.

Dr. Maryam Shanechi is pioneering work

SEE SHANECHI, PAGE 6

SEE NAGY, PAGE 8

Scholarly Publishing Symposium: Elevate Your Research Visibility

Mar. 18

The NIH Library will host a Scholarly Publishing Symposium on Wednesday, Mar. 18 from 9 a.m. to noon in Lipsett Amphitheater. Bldg. 10.

Experts will share their insights and advice on how you can make your research more visible. Topics include Author Identifiers That Improve Research Visibility (Laure Haak, executive director of ORCID); Preprints: Pros and Cons (John R. Inglis, executive director of Cold Spring Harbor Laboratory Press and *bioRxiv* co-founder, and Pritty Joshi, NIH health science policy analyst); and Social Media: How to Increase Research Visibility (César Berrios-Otero, JoVE representative and Jennifer Dorsey, NCI social media coordinator).

The event will also be videocast live at https://videocast.nih.gov/.

For more information, contact Cindy Clark at cindy. clark@nih.gov or call (301) 496-1080. Check for program details and updates at https://www.nihlibrary.nih.gov/scholarly-publishing-symposium.

New Approaches to Pain and Mental Health Featured in NCCIH Talks

This spring, the National Center for Complementary and Integrative Health offers several lectures on the theme of "Novel Approaches at the Intersection of Mental Health and Pain."



At the first talk, on Tuesday, Mar. 24, at 11 a.m. in Lipsett Amphitheater, Bldg. 10, Dr. Eric Garland will speak on "Mindfulness-Oriented Recovery Enhancement: Restructuring Reward Processing in Addiction, Stress and Pain."

In some of our most pressing "diseases of despair," such as

addiction and chronic pain, the brain's capacity to experience pleasure and extract meaning from natural sources becomes disrupted. Opioid misuse can become a way to try to hold onto a shrinking sense of well-being.

Garland has developed a nondrug intervention for opioid misuse that unites mindfulness meditation, cognitive behavioral therapy and positive psychology. A member of the NIH HEAL Initiative multidisciplinary working group, Garland is professor and associate dean for research at the University of Utah College of Social Work, director of the Center on Mindfulness and Integrative Health Intervention Development and a licensed psychotherapist. His Ph.D. in social work is from the University of North Carolina at Chapel Hill.

The lecture, which will be videocast, is part of

NIDA Director Receives AMA's Davis Award

NIDA director Dr. Nora Volkow received the American Medical Association's 2020 Dr. Nathan Davis Award for Outstanding Government Service in the category Member of Executive Branch in Career Public Service.

Recognizing Volkow's dedication to public service, the award is considered one of the most prestigious that honors local, state and federal career and elected officials. Volkow was recognized for her contributions to the field of addiction research. As one of the world's leading experts on the science of addiction, she pioneered the use of brain imaging to investigate the toxic effects and properties of drugs of abuse.

The award ceremony, held Feb. 11 at the Grand Hyatt Washington hotel, was attended by more than 500 health sector

representatives, including members of Congress and administration officials.



in the company of *ABC News* reporter Deborah Roberts and AMA board chair Dr. Jesse Ehrenfeld.

NCCIH's Integrative Medicine Research Lecture Series (see https://nccih.nih.gov/news/events/ IMlectures). Two other lectures in the series are scheduled for May 11 and June 30.

Women's History Month Workshop Set, Mar. 10 in Wilson Hall

The Office of Equity, Diversity, and Inclusion will celebrate Women's History Month with "The Whole Woman 2020 Vision Workshop" featuring keynote speaker Dr. Janine Clayton, director of the Office of Research on Women's Health. The workshop will be held on Tuesday, Mar. 10 from 1 to 3:30 p.m. in Wilson Hall, Bldg. 1.

Clayton will present
"30 Years of
Women's Health
Breakthroughs."
Other topics and presenters include views
on wellness with the
Employee Assistance
Program, mentoring
with the NIH Training
Center, FEVS data and
women at NIH with
EDI/Data Analytics.

There will also be a panel discussion on

work and life balance led by the Office of Intramural Training and Education.

Dr. Janine Clayton

Sign language interpreters will be provided. Individuals with disabilities who need reasonable accommodation to participate should contact Joy Gaines at joy.gaines@nih.gov or the Federal Relay, (800) 877-8339.

Interested in Learning How to Sail?

The NIH Sailing Association (NIHSA), an R&W supported club, offers an Introduction to Sailing course

for NIH adult employees, contractors, fellows and patients and NOAA employees. The spring course will be offered from Mar. 31 to May 12. For details, visit http://www.nihsail.org/training/.

The in-class sessions are held on the NIH campus and the onboard (on the water) sessions are held at Selby Bay on the South River near Edgewater, Md. Participants must be able to provide or arrange for their own transportation to both the in-class and onboard sessions. If you are interested in the course and would like more information, contact NIHSA at nihsabasictraining1@gmail.com.

If you are an experienced sailor and would like to charter NIHSA boats, contact the group at www. nihsail.org/rating about joining the club and doing a check-out sail. NIHSA is always looking for experienced volunteers to help with both in-class and onboard instruction.

NIH Publishes New 'NOSIs'

NIH recently published two Notices of Special Interest (NOSIs) announcing administrative supplements to expand the scope of funded investigations on U3 populations and sex/gender influences.

The first NOSI, Administrative Supplements for Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations, announces support of biomedical research highlighting health disparities among women of U3 populations.

The second NOSI, Administrative Supplements for Research on Sex/Gender Influences, announces support of research highlighting the impact of sex/gender influences in human health and illness.

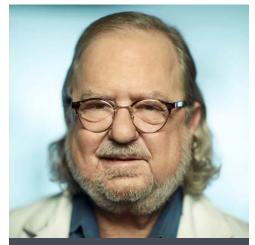
The due date for both applications is Jan. 26, 2021.

More information is available from the Office of Research on Women's Health.

WALS Talks Feature Nobel Laureate Allison, Dyer Lecturer Cooper

The NIH Director's Wednesday Afternoon Lecture Series (WALS) will host the second of three NIH Director's Lectures on Mar. 11, followed by the annual Rolla E. Dyer Lecture on Mar. 18. Both presentations are expected be held in the newly renovated Masur Auditorium, Bldg. 10, at 3 p.m.

On Mar. 11, the Director's lecture will be presented by recent Nobel laureate Dr. James P. Allison, chair and Regental professor, department of immunology at MD Anderson Cancer Center. His talk is titled



Nobel laureate Dr. James P. Allison, who speaks at NIH on Mar. 11, was the subject of a recent film titled *Jim Allison: Breakthrough*.

"Immune Checkpoint Blockade in Cancer Therapy: Historical Perspective, New Opportunities and Prospects for Cures."

Allison has spent a distinguished career studying the regulation of T-cell responses and developing strategies for cancer immunotherapy. He earned



On Mar. 18, the Dyer Lecture will be given by Dr. Lisa A. Cooper of Johns Hopkins University.

the 2018 Nobel Prize in physiology or medicine, which he shared with Dr. Tasuku Honjo, "for their discovery of cancer therapy by inhibition of negative immune regulation."

Among his most notable discoveries are the determination of the T-cell receptor structure and that CD28 is the major costimulatory molecule that allows full activation of naïve T cells and prevents anergy in T-cell clones.

Allison's current work seeks to improve immune checkpoint blockade therapies currently used by clinicians and identify new targets to unleash the immune system in order to eradicate cancer.

On Mar. 18, the Dyer Lecture will be presented by Dr. Lisa A. Cooper, Bloomberg distinguished professor, health and health care equity and James F. Fries professor of medicine at Johns Hopkins University. Her talk is titled "Deep and Wide: The Voyage to Discover Local and Global Health Equity." Cooper's research program examines the effectiveness of multilevel strategies for advancing health equity in the United States and sub-Saharan Africa. She has conducted observational studies to describe attitudinal barriers to equitable health status and health care among patients from diverse racial and ethnic groups, and to elucidate mechanisms, such as the quality of social relationships, for racial and socioeconomic disparities in health status and health care.

The Dyer Lecture was established in 1950 in honor of former NIH director Dr. Rolla E. Dyer, a noted authority on infectious diseases, and features internationally renowned researchers.

For lecture information and reasonable accommodation, contact Jacqueline Roberts, (301) 594-6747 or robertsjm@mail.nih.gov.



ON THE COVER: Near-infrared spectroscopy (fNIRS). A research participant is prepared for fNIRS, which assesses brain activation during motion capture, at the NIH Motion Analysis Lab.

IMAGE: NIH

The NIH Record

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Transit Benefit Increases for NIH'ers

The Division of Amenities and Transportation Services (DATS) announces that the mass transit benefit has increased to \$270 per month due to the recently approved 2020 federal spending bill. The increase allows NIH-eligible Transhare members to receive a transit benefit up to a maximum of \$270 per month, with no tax implications, for commuting cost coverage. The allowance does not cover parking fees.

For Transhare users, the NIH Parking Office will automatically adjust transit benefits for Transhare members who have approved commuting costs in the CAPS system greater than \$265. Transhare members should have seen this adjustment to their SmartBenefits account starting Feb. 1.

Some members who take MARC, VRE, MTA commuter bus or a vanpool will need to take additional actions to make this increase effective. An email with further instructions will be sent to those identified by DATS as taking one of these modes of transportation.

For more information, email nihparkingoffice@ors.od.nih.gov or call (301) 496-5050.



Sickle Cell

CONTINUED FROM PAGE 1

membranes distorted due to polymerization of beta hemoglobin. Like a pileup of bumper cars in an arcade, the sickled cells block traffic, leading to vaso-occlusion, a hallmark of SCD.

Sickled cells are both stiff and sticky, exhibiting abnormal adhesion, Barabino noted. "Adhesion can impede the passage of other cells, leading to obstruction, and permanent damage can result."

The interior traffic jams can include adherent reticulocytes—younger red blood cells—and white cells, said Barabino, in addition to cells that are stiffened and misshapen due to the aggregation of hemoglobin molecules. Combined, these factors result in increased blood viscosity, or thickness, and impaired blood flow.

Currently, there are two FDA-approved drugs for treating SCD, hydroxyurea and glutamine. The former appears to reduce cell adhesion within 2 weeks of administration to SCD patients, said Barabino.

There are curative therapies, too, including transfusion and bone marrow transplantation. But they are expensive and ill-suited to the low-income parts of the world where SCD is most common.

Barabino recounted attendance at an international SCD meeting held in Cotonou, the largest city in the Republic of Benin, Africa, where world leaders in SCD research met at the country's National Sickle Cell Center.

"What stood out for me was the level of incidence," Barabino said, "and the lack of access to diagnosis and treatment. There were stories of mothers who couldn't bring their children in to be evaluated. Many died before coming in for diagnosis."

To illustrate the acuteness of the suffering associated with SCD, Barabino showed a painting by Haitian artist Hertz Nazaire of a face literally blossoming with pain, watered by its own tears.

In studies of red blood cell subpopulations, Barabino and her colleagues have identified four types, distinguished by red cell density, that correlate with cell age. They have noticed the marginating of stiffer cells to vessel walls, while the more flexible cells flow within the middle of a vessel.

Their goal is to exploit this mechanical finding by extracting from blood the stiffer cells. The ability to discriminate between affected and non-affected cells also offers a way to monitor disease progression, she explained.

Her team is also studying bone involvement in SCD, which has some commonalities with osteoporosis, Barabino said. Using a transgenic mouse model of SCD that replicates the organ damage suffered by humans, the scientists are gaining insights into bone pathology.

In examinations of the microarchitecture of mouse femoral trabecular bone and cortical bone, the researchers have discovered loss of volume, thickness and strength in SCD mice as compared to controls. Bone quality rapidly declines with age, said Barabino. "Older [SCD-affected] bones are particularly deteriorated."

When her team introduced L-glutamine powder to the rodents' drinking water, the animals benefited in bone volume and reduced damage to liver and spleen.

Barabino is confident that studies of cell and tissue biomechanics will provide telltale signs of SCD progression and help investigators discriminate between health and disease.

Looking to the future, she is heartened by the NHLBI-led Cure Sickle Cell Initiative at NIH, "which links lots of partners. A comprehensive approach is needed for such a complex disorder."

There is also an American Society of Hematology SCD Initiative and a National Academies of Sciences, Engineering and Medicine Project on SCD, on whose governing committee she sits.

"That is also a very comprehensive project, and a report is due soon," Barabino said.

Media attention to SCD is also burgeoning at the moment, with the recent 60 Minutes special on NIH trials and a January article in the New York Times on a 16-year-old girl participating in the world's first SCD gene therapy trial.

"There is great promise, but a lot of unknowns," Barabino concluded, stressing the value of different perspectives when attacking a medical problem.

The full talk is available at https://videocast.nih.gov/summary.asp?live=35109&bhcp=1.





Society of Toxicology Lauds NINDS's Jett

Dr. David Jett, director of the NIH Countermeasures Against Chemical Threats (CounterACT) Program and program director in NINDS's Division of Translational Research, recently received the 2020



Society of Toxicology (SOT) Translational Impact Award.

He was recognized for his efforts to develop safer and more effective treatments for highly toxic agent exposure. He received the award Mar. 15 at SOT's annual meeting in Anaheim.

Jett earned his Ph.D. in neuropharmacology and toxicology from the University of Maryland School of

Medicine in 1992. He then conducted postdoctoral research at Johns Hopkins University Bloomberg School of Public Health, where he later joined the faculty and led a laboratory focused on organophosphorus pesticides.

Jett joined NINDS in 2002 as a program director in the Office of Minority Health and Research, working on efforts to increase diversity in the neuroscience workforce.

Based on his expertise and the events of 9/11, he soon received a request to create a program to support development of new drugs for treating victims of chemical exposures after terrorist attacks and other mass-casualty emergencies. Jett then moved to the Office of Translational Research where he designed and developed CounterACT, seeking out NIH experts from other institutes and centers to help build the program.

Since CounterACT's first year of funding in 2006, Jett and his team of NIH scientists have recruited more than 100 of the nation's top laboratories into the program, including investigators with such diverse areas of expertise as epilepsy, lung disease, dermal toxicology, ophthalmology and metabolic diseases. Their research has resulted in more than 1,400 publications in peer-reviewed journals.

The program has facilitated discovery of several promising drug candidates. One drug supported by CounterACT, Seizalam, was recently approved for treating seizures after a mass-casualty event in which nerve agents are used.

In addition to his NIH work, Jett also serves as adjunct professor in the department of chronic disease epidemiology at Yale School of Public Health and contributes his expertise to the scientific community on various advisory panels, as an editorial board member of the journal *Neurotoxicology*, guest editor for *Neurobiology of Disease* and as a reviewer for many other journals.

Get Ready for REAL ID

STARTS OCT. 1

Starting Oct. 1, NIH will no longer accept driver's licenses or other forms of identification from visitors seeking to enter campus unless those credentials are compliant with the REAL ID Act. Congress passed the act in 2005; it established minimum security standards for state-issued licenses and identification cards. As a federal agency, NIH cannot admit visitors without an acceptable form of ID.

These same standards apply to NIH staff who forget their ID badge and must access NIH facilities as a visitor.

Patients, regardless of identification, will continue to be allowed on campus upon verification of their status on a protocol with the admissions office at the Clinical Center. REAL ID-compliant forms of ID that will be acceptable for visitor admission to NIH facilities include:

- REAL ID Driver's License or State Identification Card (generally, a star in the upper right corner of the credential will indicate it is REAL ID-compliant)
 - Passport or passport card
 - HSPD-12 PIV or CAC card
 - Permanent resident card
 - Federally Recognized, Tribal-Issued Photo ID
 - · Canadian Provincial Driver's License or Indian and Northern Affairs Canada card
 - USCIS Employment Authorization card (I-766)
 - Other less common documents (e.g., Merchant Mariner credential) Some additional pointers for visitors entering NIH facilities starting Oct. 1:
 - Look for the REAL ID star on your license to make sure the license is valid
 - Children under age 17 do not need ID if accompanied by guardian with a valid ID
 - Patient caregivers will need to have valid identification
- NIH staff who forget their ID badge will need a REAL ID-compliant document to enter NIH facilities

Common reasons to obtain REAL ID include:

- You want to fly with only your state-issued ID (e.g., driver's license)
- You need to visit a secure facility, such as NIH, and do not have a personal identity verification (PIV) card, passport or another approved ID.

Reasons you may not need a REAL ID include:

- You only need your ID for purposes of identification and have another form of ID (e.g., PIV card or passport) for accessing federal facilities like NIH
- \bullet You do not mind bringing your passport along when you fly or visit federal facilities starting Oct. 1

Driver's licenses differ from state to state

REAL ID was implemented by each state's department of motor vehicles. As a result, driver's licenses and identification cards are not uniform in appearance across states. However, all REAL ID-compliant state driver's licenses will have a star imprinted in the upper right corner.

Maryland and D.C. are requiring all individuals who are eligible for REAL ID-compliant documents to obtain a REAL ID-compliant driver's license or identification card. Maryland and D.C. offer "limited use" credentials, which are not acceptable for flying domestically in the United States or for entering an NIH facility.

Virginia allows its residents the option to obtain a REAL ID-compliant credential, which can be used to enter an NIH facility. Virginia also allows a non-REAL ID-compliant credential for driver's licenses or identification cards that are not acceptable for federal purposes.



Shanechi currently is building a data-driven modeling framework that can predict how stimulation changes neural activity and thus mood symptoms.

PHOTOS: MARLEEN VAN DEN NESTE

Shanechi CONTINUED FROM PAGE 1

to model and decode mood variations, efforts that ultimately could enable modulating brain networks to treat neuropsychiatric disorders. Shanechi, whose honors include the *MIT Technology Review's* top 35 innovators under age 35, is an assistant professor of electrical engineering and neuroscience at the University of Southern California and director of USC's Neural Systems Engineering Lab. She spoke at a recent

One type of brain-machine interface (BMI) that Shanechi's lab works on allows the brain to manipulate devices, such as motor-neural prosthetics for paralyzed patients.

NIMH Director's Innovation Speaker Series

lecture in the Neuroscience Center.

"We also spend a significant amount of time developing a new generation of BMIs that aim to do the opposite," said Shanechi. "So instead of allowing the brain to control an external device, you now want to control the state of the brain itself to treat neuropsychiatric disorders, for example, using electrical stimulation."

For some patients, stimulating a certain brain region can alleviate depression symptoms. Some patients, however, don't respond to this open-loop electrical stimulation. Shanechi's team instead focuses on closed-loop stimulation, to adjust stimulation in real time based on decoding a mood state.

"We guide and stimulate the brain with the very activity we're trying to modulate and control," she said, "basically closing the loop."

This has never been done before, at least not for psychiatric disorders. Closed-loop stimulation has been successfully applied to neurological conditions such as Parkinson's disease by identifying a biomarker, and then turning stimulation on and off depending on whether the biomarker is above or below a threshold.

But mental states are largely distributed across networks, not at single sites. So a local biomarker may not work in this case. Instead, targeting mood would require decoding it by aggregating information across the network. Shanechi set out to build a dynamic model to track mood variabilities and guide how to modulate stimulation in real time within a feedback controller.

"Even if we know someone's mood perfectly, we still wouldn't know how to change it toward the therapeutic target level," said Shanechi. A neural decoder would monitor changing mood, though researchers would also need to design a feedback controller to guide the stimulation parameters toward desired levels.

Recent work with epilepsy patients showed investigators that they could decode mood variations in human subjects. Shanechi collaborated with Dr. Edward Chang, a neurosurgeon at UCSF, to obtain brain and mood data from these patients. While the patients were in the hospital getting monitored for seizures across multiple brain regions, they intermittently completed electronic mood questionnaires while hooked up to an electrocorticography (ECoG) machine. This gave Shanechi's team a data set to then start identifying specific network sites to decode and model.

With the algorithms they built for each network, Shanechi tested her model from the brain recordings of 7 people.

"In every single individual, we could significantly decode their mood variations, therefore opening the possibility of personalized therapies for mood disorders," she said.

Their decoder largely recruited the brain's limbic regions, said Shanechi, which was consistent with other studies showing the significance of these regions on emotion. As the decoders scanned patients' brains, the most recurring region was the orbitofrontal cortex.

But decoding is not enough for closing the loop, which also requires knowing how to change the stimulation for a desired outcome. Thus, Shanechi currently is building a data-driven modeling framework for this network that can predict how stimulation changes neural activity and thus the mood symptoms. To get informative data for fitting these models, "you want to stimulate the brain in a way that excites it across all frequency bands," she said. "Therefore, you want some sort of white-spectrum input, just like white noise."

She designed clinically safe white-spectrum waveforms that start with pulses, then allow for stochastic changes in amplitude and frequency to mimic white noise. Testing has already begun with encouraging results for accurately predicting how neural activity changes in response to changing stimulation. The next step is building closed-loop controllers and testing them in people. Shanechi is also working to develop multiscale models of brain network activity.

"We know that behavior involves not only small-scale neural processes measured with spiking activity of neurons," she said, "but also larger-scale integrated neural processes measured with field potentials."

The modeling challenge here is that the signals have fundamentally different characteristics. Large-scale field potentials such as ECoG are continuous with slower time scales, she explained, while small-scale spikes are binary-valued with fast millisecond timescales. The new models must describe all these signals together and account for their different characteristics.

Shanechi's lab has built a multiscale decoder that can combine information from spike-field signals at different timescales to improve accuracy and an algorithm to extract behaviorally relevant dynamics from these signals. The new algorithms are all extendable to mental states and adaptable to closed-loop control.

Shanechi continues to test these models while developing new ones, with the ultimate goal of helping us better understand dynamics across the brain that would lead to new neurotechnologies and other therapies to treat psychiatric disorders.



Webb Hooper Appointed **NIMHD Deputy Director**

Dr. Monica Webb Hooper has been selected as deputy director of the National Institute

on Minority Health and Health Disparities. Set to begin her appointment on Mar. 15, she joins NIMHD as the institute celebrates its 10th anniversary.

"I cannot express in words my elation to have the opportunity to work closely with [NIMHD director] Dr. [Eliseo] Pérez-Stable and his leadership team to contribute to NIMHD's mission and vision," said Webb Hooper, "I am deeply committed to the study of minority health

and to the ultimate elimination of health disparities. It will be a great privilege to serve NIMHD as the deputy director and to be a part of the NIH community."

Webb Hooper is a leader in minority health and cancer-related health disparities research. Her work spans multiple disparity populations, including African Americans, Hispanics/Latinos, persons of less socioeconomic privilege and people living with

HIV/AIDS. She comes to NIH from the School of Medicine at Case Western Reserve University, where she was professor of oncology, family medicine and community health, and psychological sciences. She

> also served as associate director for cancer disparities research and director of the Office of Cancer Disparities Research at the NCI-designated Case Comprehensive Cancer Center.

As a licensed clinical health psychologist, she led an active research lab focused on chronic disease prevention, health behavior change, tobacco use, weight management and obesity, stress processes, biobehavioral interventions and social

determinants of health.

Notably, Webb Hooper's group was the first to conduct a randomized intervention study of tobacco use in African Americans that effectively delineated a method to create culturally specific interventions with demonstrated long-term success. Her work highlights the importance of moving beyond one-size-fits-all approaches, particularly for behavioral interventions involving health

disparity populations.

The recipient of numerous NIH and foundation grants, Webb Hooper also has won several honors and awards for her work, including international recognition from the Society of Research on Nicotine and Tobacco.

A native of Miami, Webb Hooper has authored more than 80 peer-reviewed publications and book chapters. She earned her undergraduate degree in psychology from the University of Miami, her Ph.D. in clinical health psychology from the University of South Florida and completed an internship in medical psychology at the University of Florida Health Sciences Center. B



VOLUNTEERS

NCI Seeks Cancer Patients

National Cancer Institute researchers are testing a new treatment in people with liver cancer (hepatocellular carcinoma) or biliary tract carcinoma. The treatment uses tremelimumab given in combination with durvalumab and/ or trans-arterial catheter chemoembolization. Participants do not pay for tests, treatments or procedures. Travel may be reimbursed. Contact the Clinical Center Office of Patient Recruitment at 800-411-1222 (800-877-8339 TTY/ASCII) or prpl@cc.nih.gov. Refer to study 16-C-0135. Read more at https://go.usa.gov/xpEKb.

Patients with Anemia Sought

NHLBI is conducting an investigational treatment study with eltrombopag to help patients with Diamond-Blackfan anemia (DBA). For more information, call the Clinical Center Office of Patient Recruitment, 866-444-2214 or email prpl@cc.nih. gov, or if you need accommodation, the Federal Relay Service (https://www.federalrelay.us/federal-relay-services). Refer to study 20-H-0021. Read more at https://go.usa.gov/xdNyc.

Patients with OI Needed for Study

NICHD researchers seek individuals with osteogenesis imperfecta (OI) for study participation. Now enrolling children up to age 12 and people with OI of any age who were previously seen at NIH. For more information, call the Clinical Center Office of Patient Recruitment, 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010) or email prpl@cc.nih.gov. Read more at https://go.usa.gov/xEYjh. Refer to study 18-CH-0120.

'DEMOCRATIZING HEALTH DATA'

NIMHD Director's Seminar Hosts Boulware, Mar. 12

As part of its 10th anniversary activities, NIMHD will host Dr. L. Ebony Boulware as the next Director's Seminar Series speaker. She will present "Where Clouds Meet the Ground: Democratizing Health Data to Address Community Health Equity" on Thursday, Mar. 12 at 3 p.m. in Lipsett Amphitheater, Bldg. 10.

Boulware is the Eleanor Easley chair at the School of Medicine and chief of the division of general internal medicine in the department of medicine at Duke University.

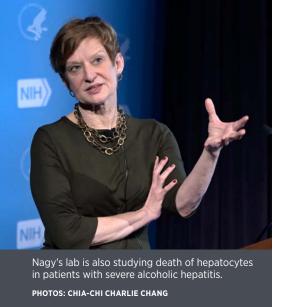
A general internist and clinical epidemiologist, Boulware empowers families and doctors with knowledge and tools to make healthy decisions and better manage chronic diseases.

The talk will be videocast at https://videocast.nih.gov.

To learn about the NIMHD Director's Seminar Series, visit https://nimhd.nih.gov/news-events/conferences-events/ directors-seminar-series/.

For reasonable accommodation, call (301) 402-1366 or the Federal Relay, 1-800-877-8339.





Nagy
CONTINUED FROM PAGE 1

Nagy, professor of molecular medicine at the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University and staff member in the departments of inflammation and immunity, and gastroenterology and hepatology at the Cleveland Clinic.

"Not all heavy drinkers progress along this timeline. There's likely an association between genetics and environment in the progression of the disease."

~DR. LAURA NAGY

*** * ***

Alcoholic liver disease is a serious health problem resulting from the overconsumption of alcoholic drinks over long periods. The liver's primary jobs are to make proteins that are essential for blood clotting and to filter blood that comes from the digestive tract and remove toxins from the bloodstream and store energy.

Patients with alcoholic liver disease first develop steatosis, the abnormal retention of fats in the liver. Steatosis is usually reversible if people reduce their consumption of alcohol. They next develop inflammation, then cirrhosis, a condition where scar tissue replaces normal liver tissue.

"Not all heavy drinkers progress along this timeline. There's likely an association between genetics and environment in the progression of the disease. This is typically a slow progression over 20 to 30 years," Nagy said.

There are several cell types that play a

role in the progression of alcoholic liver disease. One of them is the hepatocyte, "the workhorse of the liver." Hepatocytes perform key roles in metabolism, detoxification and protein synthesis.

Another is the Kupffer cell, Nagy said. They reside in a capillary called the sinusoid. A type of white blood cell, Kupffer cells are the first line of defense against bacteria and byproducts of digestion that come from the intestines, such as lipopolysaccharides (LPS).

After a person drinks an alcoholic beverage, the liver begins to metabolize and convert ethanol—the chemical name for alcohol—into acetaldehyde and then acetate. Nagy said this process produces reactive oxygen species, which leads to a "perfect storm of damaged macromolecules." Over time, the liver cannot eliminate the macromolecules.

Chronic drinking increases the amount of LPS that enter the liver from the intestines. When Kupffer cells are exposed to LPS, they release TNF- α , an inflammatory cytokine. TNF- α spurs an immune system response, which helps clear injured or dead hepatocytes. Repeated LPS exposure increases the inflammatory response.

Nagy guessed that an anti-inflammatory compound—HA 35—might be a good drug candidate for patients with alcoholic liver disease. In one animal study, her lab fed mice the equivalent of several beers per day, along with HA 35. Evidence suggested a "protective effect of HA 35" and a decrease of cytokines.

"HA 35 protects the gut and liver from ethanol" in rodent models, she said. "We've completed a safety and tolerance trial and there's potential therapeutic value, most likely in moderate disease situations."

Nagy's lab is also studying death of hepatocytes in patients with severe alcoholic hepatitis. There are several ways hepatocytes can die, including necrosis and apoptosis. Necrosis refers to cell death caused by external factors, such as an alcohol-induced injury, while apoptosis means programmed cell death. They are studying pathways that might prevent necrosis.

The Keller Lecture is a tribute to Mark Keller's pioneering contributions to the field of alcohol research. The lecture acknowledges the advances scientists are making in a wide range of alcohol-related research.

'WHAT THE EYES DON'T SEE'

Seminar by Doctor Who Exposed Flint Water Crisis

Dr. Mona Hanna-Attisha, the pediatrician and scientist whose research exposed the lead water crisis in Flint, Mich., will

be the next guest speaker in the NIMH Director's Innovation Speaker Series. Her talk, "What the Eyes Don't See: A Story of Crisis, Resistance and Hope in an American City," will be held on Thursday, Mar. 19 at 3 p.m. in Masur Auditorium, Bldg. 10. Get a



Dr. Mona Hanna-Attisha, whose research exposed the lead water crisis in Flint, Mich., will be the NIMH Director's Innovation Speaker on Mar. 19.

behind-the-scenes look at the science and continuing story of social justice behind one of the worst public health emergencies in the U.S.

Hanna-Attisha is an associate professor of pediatrics and human development and C. S. Mott endowed professor of public health at Michigan State University College of Human Medicine. She also is founder and director of the MSU-Hurley Children's Hospital Pediatric Public Health Initiative, an innovative and model public health program established to address the Flint water crisis.

In 2016, she was named one of *Time* magazine's 100 Most Influential People in the World for her role in bringing awareness to the crisis in Flint and leading the recovery efforts.

This free event is open without prior registration to all NIH staff and the public and will be webcast at https://videocast.nih.gov. For details, visit https://www.nimh.nih.gov/news/events.



A top-down view of a little-known ocean-dwelling creature most commonly found growing on dead hermit crab shells

IMAGE: ANDY BAXEVANIS, NHGRI

Study Shows How Marine Animal Produces Unlimited Eggs, Sperm Over Its Lifetime

A little-known ocean-dwelling creature most commonly found growing on dead hermit crab shells may sound like an unlikely study subject for researchers, but this animal has a rare ability—it can make eggs and sperm for the duration of its lifetime. This animal, called *Hydractinia*, does so because it produces germ cells, which are precursors to eggs and sperm, nonstop throughout its life. Studying this unique ability could provide insight into the development of the human reproductive system and the formation of reproductive-based conditions and diseases in humans.

"By sequencing and studying the genomes of simpler organisms that are easier to manipulate in the lab, we have been able to tease out important insights regarding the biology underlying germ cell fate determination—knowledge that may ultimately help us better understand the processes underlying reproductive disorders in humans," said Dr. Andy Baxevanis, director of NHGRI's computational genomics unit and co-author of the paper.

In a study published in the journal *Science*, collaborators at NHGRI, the National University of Ireland, Galway, and the Whitney Laboratory for Marine Bioscience at the University of Florida, Augustine, reported that activation of the gene *Tfap2* in adult stem cells in *Hydractinia* can turn those cells into germ cells in a cycle that can repeat endlessly.

In comparison, humans and most other mammals generate a specific number of germ cells only once in their lifetime. Therefore, for such species, eggs and sperm from the predetermined number of germ cells may be formed over a long period of time, but their amount is restricted. An international team of researchers has been studying *Hydractinia*'s genome to understand how it comes by this special reproductive ability.

Interestingly, the *Tfap2* gene also regulates germ cell production in humans, in addition to its involvement in myriad other processes. However, in humans, the germ cells are separated from non-germ cells early in development. Still, despite the vast evolutionary distance between *Hydractinia* and humans, both share a key gene that changes stem cells into germ cells.

Less Than a Quarter of At-Risk Adolescent Boys Ever Get Tested for HIV

Less than one in four adolescent men who have sex with men (AMSM) ever get tested for HIV, research funded by NIMHD has reported. The study, led by Dr. Brian Mustanski of Northwestern University, appeared Feb. 11 in the journal *Pediatrics*.

The researchers recruited 699 AMSM participants, ages 13-18 years, from an ongoing trial, called SMART, that is evaluating existing HIV prevention programs. Participants provided data on their age, race/ethnicity and place of residence. Researchers developed a questionnaire to assess their socioeconomic status and evaluate HIV transmission risk, communication with physicians and attitudes toward getting tested for HIV.

Almost half of the participants were Latino or black. Although most of the participants had a regular clinician, few had conversations with them about same-sex behavior, sexual orientation and HIV testing. The researchers also noted that older AMSM were more likely to report getting tested than their younger counterparts. Among several factors that encouraged AMSM to get tested for HIV, patient-clinician conversations were the most crucial. The researchers suggested some nonverbal ways to facilitate physician conversations, such as adaptations in the office environment to reflect inclusivity.

HIV infection goes undiagnosed in 51.4 percent of HIV-positive 13- to 24-year-olds, and 4 out of 5 new infections in this age range occur in men who have sex with men. Sexual and gender minority teenagers have a disproportionate risk of acquiring HIV because they face certain structural barriers that prevent them from getting tested. Lack of knowledge about legally being able to consent for testing and the social stigma of being outed are some of the contributing factors. This study speaks to the urgency of the Department of Health and Human Services program *Ending the HIV Epidemic: A Plan for America*, which focuses on four strategies, including early diagnosis.

Maternal Obesity Linked to ADHD, Behavioral Problems in Children

Maternal obesity may increase a child's risk for attention-deficit hyperactivity disorder (ADHD), according to an analysis by researchers from NICHD. The researchers found that mothers—but not fathers—who were overweight or obese before pregnancy were more likely to report that their children had been diagnosed with ADHD or to have symptoms of hyperactivity, inattentiveness or impulsiveness at ages 7 to 8 years old. Their study appears in the *Journal of Pediatrics*.



Researchers found that mothers who were overweight or obese before pregnancy were more likely to report that their children had been diagnosed with ADHD.

IMAGE: RAWPIXEL/GETTY

The study team analyzed the NICHD Upstate KIDS Study, which recruited mothers of young infants and followed the children through age 8 years. In this analysis of nearly 2,000 children, the study team found that women who were obese before pregnancy were approximately twice as likely to report that their child had ADHD or symptoms of hyperactivity, inattention or impulsiveness, compared to children of women of normal weight before pregnancy.

The authors suggest that,

if their findings are confirmed by additional studies, health care providers may want to screen children of obese mothers for ADHD so that they could be offered earlier interventions.

The authors also note that health care providers could use evidence-based strategies to counsel women considering pregnancy on diet and lifestyle. Resources for plus-size pregnant women and their health care providers are available as part of NICHD's Pregnancy for Every Body initiative.

NIDCR Director Somerman Celebrated Upon Her Retirement

BY ANNA MARIA GILLIS

A song, a surprise video and a story about a bear marked the retirement celebration for Dr. Martha Somerman, who stepped down as director of the National Institute of Dental and Craniofacial Research on Dec. 31 after more than 8 years of service. Speakers at the party, which was held recently in the Porter Neuroscience Research Center, highlighted some of Somerman's contributions to her field.

"We can definitely say that Martha is not a dabbler, nor has she ever been," said NIH director Dr. Francis Collins. "She has advanced the science and worked tirelessly on behalf of the dental research community and a whole generation of dental professionals."

Somerman is internationally recognized for her



NIDCR director Dr. Martha Somerman (c) watches a humorous video produced to mark her retirement.

Dr. Lawrence Tabak, NIH principal deputy director and NIDCR's acting director as of Jan. 1, described Somerman as an integrator, "one who understands multiple specialties and how they influence each other, and can foster these collaborations.

careers and to pushing for greater diversity in the scientific workforce. "Not surprisingly, a very large number of Martha's former trainees have gone on to enormously successful careers around the world." said Tabak.

Collins's song for Somerman-he often writes one for retiring directors—drew inspiration from Crosby, Stills, Nash & Young. To the tune of Teach Your Children, Collins sang:

"Martha taught her students well, and you can tell, They learn to aim high.

She mentors, she opens doors, their science soars, She takes them so high."

Somerman's penchant for running—Tabak said it was hard to keep up with her—was the inspiration for the surprise video that followed Collins's remarks. Staff from many of NIDCR's divisions and Somerman's lab participated in some variant of running on the video to honor their outgoing

And about that bear? Collins regaled the audience with a little-known fact about Somerman. When she was dean of the University of Washington School of Dentistry, one of her largest, hairiest patients was treated at Seattle's zoo. Edwina, a Malayan sun bear, broke a tooth and needed a root canal. "Martha was part of the team that treated her," said Collins.

In the coming year, while Somerman ensures her students and mice have soft transitions from her NIH lab, she "will continue to serve the human community, but I hope she will volunteer to help the National Zoo with the dental care of its residents," said Collins. "They will be fortunate bears indeed.

"Here at NIH, Martha has served with great creativity, always seeking to make something new," concluded Collins. "We are in your debt."

NICHD's Basser Honored

Dr. Peter Basser has been elected to the National Academy of Engineering (NAE) for his work in developing diffusion tensor magnetic resonance imaging and streamline tractography, which enables neurosurgeons to visualize and avoid sen-



Dr. Peter Basser

sitive structures within the brain. Diffusion tensor MRI measures the diffusion of water molecules, which can be used to probe the structure and architecture of brain tissue. It is used by neurologists and radiologists to diagnose stroke, cancer and other brain disorders. Basser is associate scientific director for imaging, behavior and genomic integrity at NICHD.

Membership in NAE honors those who have made outstanding contributions to engineering research, practice or education.

"[Martha] has advanced the science and worked tirelessly on behalf of the dental research community and a whole generation of dental professionals."

~NIH DIRECTOR DR. FRANCIS COLLINS

expertise on the regulators that control development of dental and craniofacial tissues; her intramural lab has identified genes and associated factors that promote periodontal regeneration.

Among her many accomplishments at NIH was establishing the Dental, Oral and Craniofacial Tissue Regenerative Consortium "to get research out of the lab and into the clinic and, along the way, advance the exciting and promising field of regenerative medicine," said Collins.

"Martha's NIDCR 2030 priorities have set a course for a future where dental, oral and craniofacial health and overall health will be better integrated," added Tabak. "She recognizes and encourages all of us to see how the well-being of our oral cavity links to any number of medical conditions that previously appeared to be unrelated."

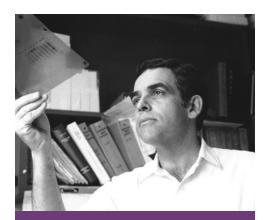
Collins and Tabak noted that Somerman has been deeply committed to training the next generation of oral health researchers at every level of their





At left, NIH director Dr. Francis Collins sings in honor of Somerman at her retirement party. At right, celebrating are (from I) Drs. Lawrence Tabak, Helene Langevin, Collins, Somerman, Bruce Tromberg and Eliseo Pérez-Stable

PHOTOS: CHIA-CHI CHARLIE CHANG



World-renowned molecular geneticist Dr. Philip Leder died Feb. 2.

Pioneering Geneticist Leder Mourned

Dr. Philip Leder, among the world's most accomplished molecular geneticists, died on Feb. 2 at age 85. His work with Nobel laureate Dr. Marshall Nirenberg—which definitively elucidated the triplet nature of the genetic code and culminated in its full deciphering—helped set the stage for the revolution in molecular genetic research that Leder himself would continue to lead for the next three decades.

Leder's scientific career at NIH and later at Harvard brought forth breakthroughs in genetic engineering, immunology and cancer research. Career highlights included the development of the first recombinant DNA vector system to meet specified safety standards, which he used to clone the gene for globin (the first cloned mammalian gene), and a series of experiments involving the c-myc gene and Burkitt's lymphoma that proved that the deregulation of a normal gene can cause cancer.

Leder first came to NIH in the 1950s as an undergraduate intern in Dr. Martha Vaughan's lab in the National Heart Institute (NHI). Upon receiving his medical degree from Harvard Medical School in 1960 and doing a residency at the University of Minnesota Hospitals, he returned to NIH in 1962, this time as a postdoctoral fellow in the Public Health Service and working in Nirenberg's laboratory in NHI's section of biochemical genetics.

In a 2012 interview with the American Society for Biochemistry and Molecular Biology, Leder described the early 1960s at NIH as the most exciting moments of his life. "I would go to bed thinking about the next day's experiments and then jump out of bed in the morning and rush to the laboratory," he said. "I stayed late at night. It was a lot of work, but the intellectual excitement was enormous."

Leder joined the Weizmann Institute in Israel as a visiting scientist in 1965 and 1966; returned to NIH as a research medical officer in the National Cancer Institute from 1966 to 1969; became head of the section on molecular genetics in NICHD's Laboratory of Molecular Genetics in 1969; and then rose to chief of that lab in 1972.

Leder taught a course on DNA replication, transcription and translation at NIH for the Foundation for Advanced Education in the Sciences. This was brand new science and the course was invariably packed. He was a chairman of the FAES department of chemistry, FAES vice president from 1970 to 1971, and FAES president from 1971 to 1973.

In 1980, Leder left NIH for Harvard Medical School, where he was founding chairman of the genetics department, a position he held until his retirement in 2008. He also became a senior researcher at the Howard Hughes Medical Institute in 1986.

Leder was recognized for his achievements with the Lasker Award (1987), the National Medal of Science (1989), the Israeli Harvey Prize (1983), the Dutch Heineken Prize (1990) and election to both the National Academy of Sciences and the National Academy of Medicine. His research supported Nirenberg's Nobel Prize in 1968, and he was a guiding force for Dr. Tasuku Honjo, his NIH postdoc in the early 1970s, who would win a 2018 Nobel Prize for cancer therapy.

Leder is survived by his wife of 60 years, Aya Leder; his children, Micki, Tani and Ben; and 8 grandchildren.



Dr. Stanley Cohen in 2007 **PHOTO: NICHD**

Nobel Laureate Cohen, Longtime NICHD Grantee, Dies

Dr. Stanley Cohen, a former researcher at Vanderbilt University and longtime NICHD grantee, died Feb. 5 at the age of 97.

Cohen's work on growth factors—naturally occurring proteins that stimulate cells to divide and form tissues—sparked a new field of science. Each growth factor has its own target receptor, a special site on the cell surface where only that growth factor will bind. Once in place, the growth

factor-receptor complex initiates signaling cascades that cause the cell to start dividing, creating new cells and tissues. Today, research on growth factors, their receptors and their activity provides potential treatment targets for cancer, severe burns and other diseases.

Cohen earned his bachelor's degree in biology and chemistry in 1943 from Brooklyn College, which he noted he could only attend "because of its no-tuition policy." He later received his master's degree in zoology from Oberlin College and his doctorate in biochemistry from the University of Michigan.

Following a brief time at the University of Colorado, he moved to Washington University in St. Louis, where he did pioneering work with Dr. Rita Levi-Montalcini. Together they isolated nerve growth factor (NGF), which enhances the growth of nerve cells, and created antibodies that inhibited NGF's activity.

Cohen became an assistant professor of biochemistry at Vanderbilt in 1959. He stayed there for more than 40 years and received funding from NICHD for most of his career, from 1964 until 1999.

At Vanderbilt, Cohen discovered, isolated, purified and sequenced epidermal growth factor (EGF), which stimulates the growth of epithelial and similar cells. He later identified EGF's target receptor and discovered its mechanism of action, specifically signaling cascades that led to cell growth.

Researchers began targeting growth factor receptors to enhance or inhibit these cascades to treat breast and other cancers, corneal ulcers and severe burns. Cohen discovered 20 other growth factors and developed a method of preventing necrotizing enterocolitis in a rodent model.

In 1986, Cohen and Levi-Montalcini earned the Nobel Prize in physiology or medicine and the Albert Lasker Basic Medical Research Award for their growth factor discoveries. Cohen received the National Medal of Science the same year. He was elected to the National Academy of Sciences in 1980 and the American Academy of Arts and Sciences in 1984. He retired from Vanderbilt in 2000 as distinguished professor emeritus of biochemistry.

NICHD recognized Cohen in 2007 for his many discoveries on growth factors, including his NICHD-funded discovery of EGF, with a Hall of Honor Award. This award program, which ran from NICHD's 40th anniversary in 2003 through 2010, honored individuals who exemplified scientific curiosity and service to others.

Cohen had been living at a retirement community in Nashville for several years. He is survived by his wife, his two children and stepchild from his first marriage and two grandchildren.





'PuppyCam' Event Brings Fur, Fun to Campus

PHOTOS: CHIA-CHI CHARLIE CHANG

For the third year in a row, NIH hosted PuppyCam, a live event held Feb. 13 in conjunction with Hero Dogs, Inc., an organization that "improves quality of life for our nation's



heroes by raising, training and placing service dogs and other highly skilled canines, free of charge with lifetime support of the partnerships."

The event is also sponsored by the Children's

Inn at NIH, whose on-site companion dog Zilly oversees the affair.

Throughout the event held on the FAES Terrace in Bldg. 10, NIH live-streamed on Twitter a group of service-dogs-in-training and therapy dogs while NIH experts gave brief talks on mindfulness, stress reduction and pet therapy.

Two-legged participants included NIH director Dr. Francis Collins, NIDDK director Dr. Griffin Rodgers, NHGRI director Dr. Eric Green, NCCIH director Dr. Helene Langevin and other leading NIH scientists.

There were 30,000 live views, and the video had nearly 47,000 views and was still growing on Twitter just days after the event.



Pumped for puppies. NIH director Dr. Francis Collins (I and above) makes new friends at the event. Below, NIDDK director Dr. Griffin Rodgers cuddles a Hero Dog.





Above, NHGRI director Dr. Eric Green permits a pup's smooch. At right, NIDCR's Drs. Melissa Riddle (I) and Elise Rice enjoy the puppies.

