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Range of Issues Considered at 116th ACD Meeting

BY RICH MCMANUS

Although NIH director Dr. Francis Collins instantly accepted the unanimous recommendation of the 116th gathering of the advisory committee to the NIH director that NIH begin at once to terminate NIAAA's 10-year, \$88 million Moderate Alcohol and Cardiovascular Health (MACH) study due to numerous departures from established norms governing public-private partnerships, much else occupied the ACD during its semi-annual deliberations June 14-15.

"It's been a pretty intense 6 months since we last met," said Collins at the outset of a meeting that traditionally displays the breadth and depth of agency concerns.



NIH director Dr. Francis Collins at ACD meeting

In just a day and a half, the group reviewed at least a dozen major issues, including:

• The 15 themes that make up the \$500 million HEAL (Helping to End Addiction Long-term) Initiative that NIH has

Wenger Puts Women at Heart

National Institutes of Health

embarked upon to address the nation's epidemic of opioid misuse and abuse. "This crisis is not going to be solved by any single intervention," said Collins, noting that opioids were responsible for more than 42,000 deaths in 2016 (some 20 percent of which may have been suicides, added NIDA director Dr. Nora Volkow).

· Personnel actions, including nationwide searches for new directors of NIBIB, NIDCD and NCCIH, plus a new chief data strategist-preferably one with Silicon Valley expertise, Collins noted-to help make sense of the information tsunami generated by the more than 25 million people participating in cohort studies worldwide.

• A précis of NIH's response to the most recent outbreak of Ebola in Africa, offered by NIAID director Dr. Anthony Fauci, who lauded NIH's "ability to hit the ground running when called upon in an emergency SEE ACD MEETING, PAGE 4

AT-WORK WORKOUT **High Spirits, Low Stress Mark** 'Take a Hike Day'

BY CARLA GARNETT

Normally, when more than 1,300 employees walk off the job mid-day, a workplace has a



ORS's Joe Cox and Cpl. Christine Fedorisko form cheering squad at hike.

problem. That is, unless it's NIH's annual Take a Hike Day, when the boss actually encourages the at-work workout.

"Are you ready to walk, run and absolutely take advantage of this beautiful day?" enthused NIH director Dr. Francis Collins, briefly taking the

Of Research BY DANA TALESNIK Heart disease still tops the list of the

leading causes of death for men and women in the United States, yet women tend to be affected later in life and often have different symptoms than men. Only half of women who have heart attacks experience chest pain, for example.



Dr. Nanette Wenger

Women typically report other symptoms such as back pain, heartburn, nausea, extreme fatigue and/or difficulty breathing.

Despite the differing symptoms and risk

Asian heritage fashions featured. See p. 12.

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BRIEFS

NINDS, NIMH To Host Kopin Memorial Symposium, July 26

NINDS and NIMH will host a symposium on Thursday, July 26 at Natcher Conference Center: "Catecholamine Research: The Enduring Impact of Irv Kopin," a 1-day memorial event honoring the



late Dr. Irwin J. Kopin. He was a scientist emeritus, former chief of NIMH's Laboratory of Clinical Sciences and retired NINDS scientific director. His groundbreaking research on the characteristics and metabolism of catecholamines hormones made

by the adrenal glands that include epinephrine (adrenaline), norepinephrine and dopamine provided the backbone for major advances in neurological and psychiatric disorders.

The symposium will feature a series of stateof-the-art lectures by world authorities in the catecholamine research field and a poster session that will provide a unique opportunity for multiple generations of catecholamine researchers to meet and interact in a collegial setting. Interested NIH scientists should send poster abstracts to Dr. David Goldstein at goldsteind@ninds.nih.gov. Visit https://meetings.ninds.nih.gov/meetings/kopin/ to learn more and register.

Garraway To Give NCI Seminar, July 24

Dr. Levi Garraway is the featured guest speaker for the next lecture in NCI's Center to Reduce Cancer Health Disparities' Continuing Umbrella of Research



Experiences (CURE) Distinguished Scholars Seminars on Tuesday, July 24 from 2 to 3:30 p.m. at the NCI Shady Grove campus, Rm. TE406. The title of his lecture is "Molecular and Genomic Characterization of Human Solid Tumors."

Garraway is senior vice president of global oncology and medical affairs at Eli Lilly and Co., associate professor of medicine in the medical oncology service at Dana-Farber Cancer Institute and the Broad Institute. He is also director of the Joint Center for Cancer Precision Medicine and co-leader of the cancer genetics program at Dana-Farber/Harvard Cancer Center.

Garraway has served on national and international committees including former Vice President Biden's blue ribbon panel to develop recommendations



CDC Director Redfield Visits NIH

Dr. Robert Redfield, the 18th director of the Centers for Disease Control and Prevention and a longtime HIV researcher, visited NIH on June 12. He met with NIH senior leadership about opioids, the BRAIN Initiative and neuroscience and a universal flu vaccine. Above, at the Vaccine Research Center, Redfield (I) and Amanda Campbell, CDC deputy chief of staff, meet with (from I) NIAID director Dr. Anthony Fauci, VRC director Dr. John Mascola and NIH director Dr. Francis Collins. Below at left, Redfield, whose parents worked in Bldg. 10 years ago, views the CRC model with hospital CEO Dr. James Gilman (I), Collins and Fauci. Below at right, Redfield tours the special clinical studies unit with Fauci and Dr. Richard Davey, who oversees the unit.

PHOTOS: CHIA-CHI CHARLIE CHANG



for the Cancer Moonshot Initiative. He currently serves on the American Association for Cancer Research (AACR) board of directors and in 2016 was president of the American Society of Clinical Investigation—one of the highest honors for academic clinician-scientists.

The author of nearly 200 peer-reviewed scientific articles, Garraway has received several awards, including the Paul Marks Prize for Cancer Research, the Jane Cooke Wright Award from AACR, NIH's New Innovator Award and an Outstanding Investigator Award from NCI. His industry activities include founder of Foundation Medicine, a leading company in cancer genomics diagnostics.

Internationally recognized for his work on genomic alterations in cancer for the purpose of identifying therapeutic interventions, Garraway received his M.D. and Ph.D. degrees from Harvard Medical School.

To register for the seminar via WebEx, visit https://bit.ly/2KuF17P. For reasonable accommodation, call (301) 402-1366 or the Federal Relay (1-800-877-8339).



Graduate & Professional School Fair

July 18

The 2018 NIH Graduate & Professional School Fair will be held on Wednesday, July 18 from 8:45 a.m. to 3:30 p.m. at Natcher Conference Center. The fair provides an opportunity for NIH summer interns (especially those in college) and postbacs, as well as other college students in the D.C. area, to prepare for the next step in their careers by exploring educational programs leading to the Ph.D., M.D., D.D.S., M.D./Ph.D. and other graduate and professional degrees.

The day will also include workshops on getting to graduate and professional school; M.D./Ph.D. programs; interviewing; and careers in public health, computational biology/bioinformatics, psychology and dentistry. Exhibits will be open from 9:45 a.m. to 2:15 p.m.

A list of institutions planning to attend and registration information can be found at https://www. training.nih.gov/gp_fair.

NIH RECORD

ALONG THE GUT-BRAIN AXIS

Alcohol, Sleep and the **Microbiome**

BY FRIC BOCK

Many people who regularly drink large amounts of alcohol have chronic sleep problems. By learning about the composition of the bacteria and other single-celled organisms in their digestive systems, researchers in the Clinical Center hope to develop treatments to help these patients sleep, said Dr. Alyssa Brooks during a recent Clinical Center Grand Rounds lecture in Lipsett Amphitheater.

"Alcohol affects sleep," said Brooks, scientific program specialist in the CC's nursing department. "The relationship between the two constructs is complex and alcohol can accelerate the onset of sleep, but disrupt sleep later in the night."

Not getting the recommended 7 or more hours of sleep per night can lead to long-term health problems and dangerous behavior such as drowsy driving, she said.

People with alcohol use disorders (AUD) experience sleep disturbances throughout the night.



to fall asleep than people who drink only occasionally or not at all. AUD is a condition where a person drinks alcohol that 90 percent compulsively, cannot of patients in the control how much he or she drinks and feels anxious, irritable or stressed when sober.

They take longer

Heavy alcohol use also affects a person's microbiome, participants were which refers to "the

genome of all microorganisms within humans." Much of a person's microbiome is located in the gut. Diet, age, environment and medications influence the microbiome's makeup.

Patients who consume alcohol chronically have a significantly different microbiome compared to healthy populations. These changes are associated with depression and alcohol craving that can eventually lead to relapse.

"We now understand there's what we call the gut-brain axis." Brooks explained. This refers to communication between the gut microbiota and the brain. The axis can influence anxiety, depression and behavior.

To learn more about the potential link between alcohol and the microbiome, Brooks helped design two studies of patients from the CC's treatment unit for patients with alcohol use disorders. One



Dr. Alyssa Brooks (I) and Dr. Nancy Ames at rounds PHOTOS: MARLEEN VAN DEN NESTE

> examined sleep disturbance among individuals with AUD throughout recovery, while the other examined changes in the oral/gut microbiome among individuals with AUD.

There would be no study were it not for the nurses on the unit who "recognized the need for assessing sleep extensively in this patient population," Brooks noted.

The research team used both subjective and objective measurements, including the Pittsburgh Sleep Quality Index, to assess a patient's sleep. The PSQI is a self-reported assessment that measures sleep quality over the course of one month. Investigators

in the nursing department found **Clinical Center's** AUD unit reported sleep disturbances when they first entered inpatient treatment.

Many of the anxious about moving from inpatient to outpatient treatment, Brooks noted. According

to the objective measures of sleep, the patients slept only 65 percent of the time they were in bed in the week preceding discharge. After patients were discharged from the unit, sleep disturbances continued in about half the patients.

She cautioned that results of the study are preliminary and there's still a "wealth of information" awaiting analysis.

While undergoing treatment, patients enrolled in the study examining changes in the oral/gut microbiome submitted stools samples for genetic sequencing, said Dr. Nancy Ames, a nurse scientist in the nursing department's nursing research and translational science section.

Six patients who were enrolled in both studies provided a stool sample every day for the first week of treatment. After that, each person submitted one stool sample for another 3 weeks. The research team collected an oral sample by swabbing patients' tongues. Patients also kept a food log for 4 weeks.

Before the results came in, Ames assumed the composition of the microbiome would change while patients recovered from the disorder. That wasn't the case, however. Preliminary data suggest the microbiome didn't change significantly during their stav at the CC.

"It's pretty remarkable it didn't change that much," she said. "That's the story."

Further analysis might lead to more insights. Next, Ames plans to work with dietitians to analyze food logs of patients being treated for AUD. "We have a lot of work to do," she concluded. R



ON THE COVER: Recent NCI cryo-electron microscopy study reveals the structure of the light-sensing G protein-coupled receptor rhodopsin. captured in a signal transduction step.

IMAGE: VERONICA FALCONIERI & SRIRAM SUBRAMANIAM, NCI

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National Institutes of Health Turning Discovery Into Health

ACD Meeting CONTINUED FROM PAGE 1

situation." Ironically, the current, limited outbreak—one of 24 that have occurred since 1976—is affecting the Democratic Republic of the Congo, formerly known as Zaire, host of the world's first recognized outbreak. The current outbreak is the country's ninth.

• Optimism about NIH budgets that, in the past 3 years, have risen a total of \$7 billion, which has put a major dent in the 22 percent loss in inflation-adjusted dollars that NIH experienced between 2003 and 2015. NIH is now only 11 percent behind its FY 03 purchasing power, and on June 14, the House proposed a \$1.25 billion increase for NIH in FY 2019.

• The Next Gen Researchers Initiative is fine-tuning its focus on early-stage investigators, with a goal of increasing their number from 1,040 to 1,100 in the coming fiscal year, with help flagging at-risk scientists to take place in the meantime. "We're not waiting until December [when the Next Gen working group issues its final report]," Collins noted.

• A new NIH anti-harassment policy governing both intramural and extramural behavior that will debut this summer. "I am embarrassed by the fact that our advisory committee to the director is so unbalanced with respect to gender," said Collins at the start of the discussion, adding that he will make it his highest priority to correct the situation. Dr. Lawrence Tabak, NIH principal deputy director, serves as chair of the NIH anti-harassment steering committee and outlined features of the new policy.

• Also shy in attracting women have been some of NIH's high-risk, high-reward grant programs; discussants wondered if some of the language in FOAs—funding opportunity announcements—has been off-putting to potential female candidates.

• The BRAIN Initiative, begun in 2013, is now maturing to BRAIN 2.0, to be presented in final form next June. The funding has been ramping up. Thus, at the halfway point of its 10-year tenure, only 11 percent of its funds have been obligated, said NIMH director Dr. Josh Gordon. BRAIN is only about 10 percent of NIH's overall neuroscience spending, said Collins. NINDS director Dr. Walter Koroshetz expects recent scientific advances "to put electrodes out of business" as precision circuit modulation of specific cell types becomes possible.

• Upwards of 25 million Americans suffer chronic pain daily, Koroshetz reported, adding, "It's pretty clear we have inadequate treatment...We have terrible treatments for people with chronic pain." Opioids will need to be displaced from the pharmacopeia, he said. "[Understanding] the basic science of pain has exploded in the last few years," Koroshetz noted. "There are valuable assets out there that need testing."

• A dearth of women and underrepresented minorities in the scientific workforce is still a burning issue, said Dr. Hannah Valantine, NIH chief officer for scientific workforce diversity; academia is not "pulling" well-trained members of this population into the ranks of tenured professorship. "Changing the culture to be more hospitable requires real commitment," she told the group.

And then there was the MACH study designed as a multicenter, randomized clinical trial to determine the effects of one serving of alcohol (approximately 15 grams) daily, compared to no alcohol intake, on the rate of new cases of cardiovascular disease and the rate of new cases of diabetes among participants free of diabetes at baseline. The study came into question via news reports published last March.

Initially funded in September 2016 [some

\$68 million from the beverage industry, via the Foundation for the National Institutes of Health, with NIAAA committing \$20 million over 10 years—only \$16 million had been spent, in total, so far] MACH was suspended by NIH on May 10 for ethical lapses. Scrutinized by both NIH's Office of Management Assessment and an ACD working group, the study, which had already recruited 105 subjects, starting last February, was found to have crossed multiple ethical lines, Collins said. "It's doubtful that study results could ever have been credible."

"I must say I'm disappointed with what transpired," said NIAAA director Dr. George Koob. He acknowledged "design issues and significant process irregularities that undermined the integrity of the research... The study is irrevocably damaged and we cannot justify continuing."

"Purely on scientific grounds, I never really quite understood why this trial was being done," said ACD member Dr. M. Roy Wilson, president of Wayne State University, especially with the opioid issue going on. "There are many of us, including me, who will take a drink or two of wine a day. We don't do it for health reasons. The results of the trial just wouldn't have influenced me one way or the other."

Collins emphasized that "most public-private partnerships are greatly beneficial and above reproach," mentioning efforts in



"I haven't seen it done better," said ACD member Dr. Mark Dybul (r), professor of medicine at Georgetown University, of NIH's handling of the MACH study. "I've sadly been involved in [review of] way too many issues like this." At left is ad hoc ACD member Dr. Francis Cuss.

PHOTOS: ANDREW PROPP

CROSSING CHIASM



Said ACD member Dr. M. Roy Wilson, "There are many of us, including me, who will take a drink or two of wine a day. We don't do it for health reasons. The results of the [MACH] trial just wouldn't have influenced me one way or the other."

Alzheimer's disease, diabetes, lupus, cancer and Parkinson's disease, among others. "We want to avoid putting tar on our brush and spreading it around indiscriminately."

He said MACH provided a "teachable moment" and acknowledged that "clearer boundaries are needed...We need to understand what appropriate behavior is. But we don't want an investigative culture, either."

Collins called for 60 days of information-gathering on all NIH studies involving non-federal funding. "This was an unusual outlier," he said, "but we need to be sure… We need to reinforce standards of ethical behavior across NIH."

The issue will be revisited at the next ACD meeting in December, Collins said. "We will report on what we've found and what actions we will take...This is a matter of the greatest seriousness. We will not just be checking a box and saying 'We took care of that.' We need to live up to the principles of openness and fairness, which are a mainstay of our integrity. Anything that compromises that is unacceptable."

At a media session on MACH following the conclusion of the ACD meeting, Tabak noted that "a small number of employees violated NIH policies" and that "appropriate personnel actions will result.

"This isn't an indictment of industry engagement," he said. "It's an indictment of the way this one was conducted."

Mason Offers Lessons in Axon Guidance For Binocular Vision

BY LESLEY EARL

Retinal neurons are programmed to migrate to one side of the brain or the other during development. Dr. Carol Mason of Columbia University, who recently visited NIH, has discovered elements of this programming. Understanding the factors that guide neurons to their appropriate targets could someday help doctors rebuild damaged visual circuitry in the brain.

Millions of years ago, sometime between the appearance of fish and frogs on the planet, animals' connections between the eyes and the brain transitioned from a simple crisscross (right eye to left brain, and vice versa) to a more complex arrangement.

Binocularity, as it's called, evolved when each eye began connecting to both sides of the brain, enabling the brain to merge input from both eyes into a single image. Increased binocularity is found in animals, including humans, with eyes close together on the front of the head, and is needed for depth perception.

During development, neurons grow out of the retina toward the brain, passing through a zone known as the chiasm. In certain animals such as fish, all neurons from the retina are contralateral, meaning they cross the chiasm. In higher-order species, including mice and humans, a subset of retinal neurons do not cross the chiasm, instead connecting to the same side of the brain as the eye from which they originate. These are called ipsilateral neurons.

For Mason, there are two big questions: How are contralateral and ipsilateral neurons different? And what factors determine the direction neurons go when they reach the chiasm?

Using mice, she found that the neurons destined to cross the chiasm carried one set of protein markers on their surfaces, while those programmed to reverse course carried a distinct set of protein markers. In effect, the cells of the chiasm acted as filters, repelling the ipsilateral neurons while allowing the contralateral neurons to pass through.



Each group of neurons—generally depending on where they start in the retina—are pre-programmed to become contralateral or ipsilateral. But, curiously, in people lacking

the tyrosinase gene, some ipsilateral neurons cross the chiasm incorrectly. These people end up with too many contralateral neurons, which results in poor stereo vision (including reduced depth perception). By tracking individual neurons, Mason discovered that a specific group of neurons, originating from a particular region of the retina, are the ones that lose their way.

Tyrosinase isn't involved directly in neuron growth or the chiasm. Instead, tyrosinase is critical for producing melanin, the pigment found in skin and in retinal epithelial cells.

"It's still a mystery," said Mason. "Why does the absence of melanin produce a reduction in the ipsilateral pathway?"

Understanding how these neurons connect is critical for understanding how to rebuild those connections after the retina has degenerated from diseases such as glaucoma and age-related macular degeneration.

"The one big bugaboo in all of retinal regeneration *in vivo*," said Mason, "is that nothing can get through the optic chiasm in the adult." Knowing how these neurons find their way could be key to restoring vision in adults who have lost their sight.



At left, it's all smiles and optimism at the starting line. At right, NIH director Dr. Francis Collins encourages hikers to enjoy their splendid surroundings along the way. PHOTOS: MENA BRUNETTE

Hike CONTINUED FROM PAGE 1

podium set up in front of Bldg. 1 June 7 to cheer on participants.

Describing himself as "a little bit of a fitness nut," Collins said he envied employees who were able to arrange their schedules and put NIH's health and fitness messages into action. He had a meeting downtown and could not take part.

Collins also suggested that those participating capitalize on their good fortune to be able to work at such a scenic locale. Recalling the rich history of NIH's formerly rural Bethesda campus, he said there are more than 8,000 trees of 150-plus species currently amid the 300 acres where more than 50 species of birds have been spotted. He also acknowledged other wildlife that have been documented in the vicinity such as deer, Canada geese and even a bear once a few years ago. It was "exactly 80 years ago this month [June 1938] that the cornerstone [of Bldg. 1] was laid," Collins recalled.

Quoting President Franklin Roosevelt when he visited NIH in 1940, Collins said the institution was "dedicated to the underlying philosophy of public health, to the conservation of life, to the wise use of the vital resources of our nation.' That's what you all have been doing and that's what you're doing today. I think we've lived up to Roosevelt's best hopes...Enjoy the opportunity to appreciate where we are...We exist here on a perfectly beautiful campus."

Tim Tosten, acting director of the Office of Research Services, launched the event, which starts on the front lawn of Bldg. 1, heads down Wilson Drive and outside the perimeter fence onto Rockville Pike.

Welcome to the 11th annual Take a Hike Day, Tosten said, when we "dedicate time to take our own best advice and encourage healthy behaviors among our federal workforce. Not only does this event promote physical fitness, but also it promotes social interaction, provides community and promotes well-being."

Tosten recalled that Tom Hayden, the late ORS Division of Amenities and Transportation Services director, developed the hike in 2008 for employees as "a way to get moving and foster *esprit de corps* of the NIH family." That year, the event was held in May in conjunction with the National President's Challenge and the HealthierFeds initiative.

An estimated 15,500 employees have taken a hike since its inception 10 years ago. The event has expanded to include satellite versions where other NIH'ers work— Executive Plaza, Fishers Lane, Rockledge and Shady Grove.

"We've seen an increase in participation at off-campus locations such as Fishers



At left, runners lead off. At center, returning hikers wave. At right, NIH Fitness Program instructor Linda Bessacque leads vigorous warm-up before the hike.



At left, the DATS crew, who bring the hike to life every year, gather for a photo after the event ends. At right, Tim Tosten, acting ORS director, gives the hike's ground rules.

Lane and Shady Grove," noted Shuntrice Holloman of DATS, which organizes the event.

Tosten also noted that the hike this year is part of an overall NIH strategy for its employees to address five tenets of well-being—community, social, work, physical and financial health.

"The hike incorporates 3 of the 5, so you're well on your way to adopting all 5," he concluded.

Perfect weather and bucolic setting aside, the 3.25-mile loop around the campus can still pose a challenge for some normally sedentary souls.

"Okay, we're starting to climb a little hill here," announced a cheery strider, approaching the event's first incline.

"You're calling this a 'little hill?" quipped a fellow walker.

"It's all relative, isn't it?" strider one shot back, to laughs from those alongside.

The walk's first leg also found itself navigating around an in-process construction site at the Metro intersection at Rockville Pike and South Drive. NIH Police directed traffic and held off vehicles for pedestrians crossing the area. By the second turn, back into the wooded environment near the National Library of Medicine, the street noise fell away and a park-like atmosphere enveloped walkers. It's by far the sweetest portion of the course—unless you count the almost totally downhill stretch of Cedar Lane.

At water station one, which was sponsored by the Office of Research Facilities and ORF Director Dan Wheeland, volunteers Mahmoud Solhdoust and Terence Lewis welcomed walkers looking for water and a short breather. Other stations were hosted by the cross-institute/center NIH Health & Wellness Council as well as various other ICs. NIA's Jamie Goldsby and NHLBI's Kathryn McMurry of the council enthusiastically waved walkers to their station along Old Georgetown Rd.

Organizers report 1,334 registered participants, including 1,080 walkers and 254 runners. NIAID registered the most people at 246, with OD second at 200 and NCI third with 182. About 30 volunteers helped out in various capacities. As for the number of overall attendees?

"We're still trying to figure that number out," said Holloman.

> By event's end, the crew running things had recorded another successful day, with the spirit of collegiality continuing into the afternoon: As DATS gathered for a photo, a still highly energetic group from Medical Arts/Division of Scientific Equipment and Instrumentation Services took over sign-waving, high-fiving and overall cheerleading duties at the finish line.

Cheng Named Chief of CSR Review Group

The Center for Scientific Review has named Dr. Yuanna Cheng as chief of its surgical sciences, biomedical imaging and bioengineering integrated review group. She had been acting chief and previously served as scientific review officer for the clinical and

integrative cardiovascular sciences study section and the electrical signaling, ion transport and arrhythmias study section.

"Since coming to CSR in 2011, Yuanna has demonstrated a keen ability to understand, communicate and implement policy to drive the highest quality of review," said acting CSR



director Dr. Noni Byrnes. "She is a member of the CSR's best practices committee and has been a key resource for CSR leadership in the implementation of the new NIH clinical trials policies."

Byrnes also noted that Cheng is well-suited to lead this review group due to her broad clinical background along with her research experience in using advanced imaging modalities and her previous involvement in training the next generation of biomedical engineers.

Cheng will oversee six standing study sections and numerous special emphasis panels that review a broad range of NIH grant applications.

She received an M.D. at Tongji Medical University in China and a Ph.D. in physiology at the Medical College of Oita in Japan. This was followed by a postdoctoral fellowship in the division of cardiology at the University of Pittsburgh. She was then recruited to the Cleveland Clinic, where her research focused increasingly on translational aspects of cardiac electrophysiology.

Before joining CSR, Cheng was associate staff in the department of cardiovascular medicine and department of molecular cardiology at Cleveland Clinic as well as an adjunct associate professor in the department of biomedical engineering at Case Western Reserve University.



If you're having fun at work today, raise your hand!

Wenger CONTINUED FROM PAGE 1

factors of coronary heart disease among men and women, this life-changing—often life-saving—information wasn't known for many decades because clinical cardiovascular studies didn't include women.

One medical pioneer who sought to change that predicament is Dr. Nanette Wenger, who recently spoke at an NHLBI seminar, part of a series to celebrate the institute's 70th anniversary.

Wenger, professor of cardiology at Emory University School of Medicine, is one of the first American doctors to focus on heart disease in women. Since graduating from Harvard Medical School in 1954, she has devoted much of her career to helping unclog the arteries of the male-dominated field of cardiology.

"We've come a long way, baby!" Wenger exclaimed, after showing an American Heart Association ad from the 1960s that urged women to prepare heart-healthy meals for their husbands. In 1964, in Oregon, participants at the first women's conference on heart disease discussed a woman's responsibility to care for her husband.

Perhaps those healthier meals made a difference. The mortality rate among men with cardiovascular disease was steadily declining from 1979 to 1998, but the rate remained unchanged for women, said Wenger. Over the last 20 years, though, the statistics started to change, thanks to science-based evidence for preventing, diagnosing and managing heart disease among women.

"Since 2000, there's been a precipitous decline in cardiovascular mortality in women, a decline much more prominent than in men," said Wenger. "In 2015, for the first time since 1984, fewer women than men in this country died from cardiovascular disease. We're delighted to be in second place and hope to remain there."

Several evidence-based reports and conferences since 2000 have identified knowledge gaps, largely due to recommendations and guidelines for women that were extrapolated from men's studies. Wenger underscored the need to disaggregate study results and report gender-specific analyses from clinical trials. One landmark event came in 2001 from the Institute of Medicine report *Does Sex Matter*? Before this report, and the HERS and WHI hormone trial results, said Wenger, "Women were considered protected from heart disease by their hormones." Randomized controlled trials soon would find that the supposedly cure-all menopausal hormone replacement therapy did not prevent heart disease, or any other chronic illness for that matter.

Said Wenger, "This was enormously important because it refocused attention on the established cardiovascular preventive therapies for women, no longer the

reliance on unreliable menopausal hormone therapy." Studies then appeared debunking the notion that vitamins, including folic acid and beta carotene, prevent cardiovascular disease. "Women were absolutely enamored

*** * ***

"Heart disease in women is not solely a medical problem and we have to be much more inclusive in our approach."

~DR. NANETTE WENGER

* * *

with their vitamins. When the results of these studies came out," recalled Wenger, "my clinicians would tell me how much difficulty they had trying to wean women off these non-helpful therapies and onto beneficial therapies."

Historically, gender medicine focused on what Wenger calls "bikini research"—the breasts and reproductive system—the parts covered by a bikini. As the areas of women's research expanded, so too did awareness campaigns such as NHLBI's Heart Truth and AHA's "Go Red for Women," which made the red dress a universal symbol of women's heart health.

In recent years, guidelines began emerging to screen women based on risk factors such as pregnancy complications. Such conditions as gestational diabetes, preeclampsia and pregnancy-induced



Wenger is one of the first American doctors to focus on heart disease in women. PHOTOS: LISA HELFERT

hypertension can be early indicators of cardiovascular risk, said Wenger. Identifying such risks can help doctors intervene earlier, if necessary.

Now, more attention is given to comorbidities such as diabetes, stroke and clinical depression. Recent studies have shown, for example, that lifestyle interventions seem to improve cardiovascular mortality more in pre-diabetic women than in pre-diabetic men.

Another area of concern is breast cancer treatment, which, although curative for breast cancer, can put women at risk for long-term cardiac complications. "We need surveillance, prevention and secondary management of cardiotoxicity during breast cancer treatments," said Wenger.

Despite growing awareness and focus on women's heart health, women continue to be underrepresented in cardiovascular research as well as undertreated, said Wenger. She argued for more public health campaigns that target racial and ethnic minority women, who have the highest number of cardiovascular-related mortalities.

Wenger said her vision for the next decade is to see women's cardiovascular health further expanded to incorporate beliefs and behaviors as well as economic, environmental, ethical, political and sociocultural issues.

"Heart disease in women is not solely a medical problem," said Wenger, "and we have to be much more inclusive in our approach."

After Wenger's presentation, she did a sit-down chat/Q&A with NHLBI senior scientist & chief of staff Dr. Nakela Cook.

DIGEST

FEEDBACK

Study Associates Obesity with Lower Breast Cancer Risk in Young Women

Young women with high body fat have a decreased chance of developing breast cancer before menopause, according to scientists at NIH and their collaborators. The finding, published online in the journal *JAMA Oncology*, may help researchers better understand the role obesity plays in breast cancer risk.

"It is well known that women who gain weight, particularly after menopause, carry an increased risk of postmenopausal breast cancer," said Dr. Dale Sandler, co-senior author and head of NIEHS's Epidemiology Branch. "Our finding that breast cancer risk is not increased in obese premenopausal women, and in fact



Study finds that different biologic mechanisms may be responsible for causing breast cancer in younger women. IMAGE: WITTHAYA/THINKSTOCK

decreases, points to the possibility that different biologic mechanisms are responsible for causing breast cancer in younger women."

Sandler said since the development of breast cancer is relatively rare before menopause, researchers previously found it difficult to fully evaluate risk factors in a single study. She added that previous studies suggested risk factors for breast cancer in younger women may not be the same as in older women.

To understand breast cancer risk in women who have not gone through menopause, Sandler and other researchers formed the Premenopausal Breast Cancer Collaborative Group. The international team pooled data from 19 different studies, comprising 758,592 women from around the world. The approach allowed the team to identify risk factors and patterns that would be difficult to detect with a smaller number of women.

While Sandler and her colleagues are unsure why young, premenopausal women with a high BMI appear to be protected against breast cancer, she cautions that young women should not intentionally gain weight to lower their breast cancer risk.

"There are so many health risks associated with being overweight or obese," Sandler said. "We still believe it is important for women to maintain a healthy weight throughout life."

Two Diabetes Meds Don't Slow Progression of Type 2 Diabetes in Youth

In youth with impaired glucose tolerance or recent-onset type 2 diabetes, neither initial treatment with long-acting insulin followed by the drug metformin, nor metformin alone preserved the body's ability to make insulin, according to results published June 25 in *Diabetes Care*.

The results come from a study of 91 youth ages 10-19, part of the larger Restoring Insulin Secretion study. To determine if early, aggressive treatment would improve outcomes, participants at 4 study sites were randomly assigned to 1 of 2 treatment groups. The first received 3 months of glargine—a long-acting insulin—followed by 9 months of metformin. The second received only metformin for 12 months. Participants were then monitored for 3 more months after treatment ended.



Research suggests type 2 diabetes in youth may be more aggressive than in adults.

IMAGE: TOMWANG112/THINKSTOCK

The RISE Pediatric Medication Study found that beta cell function—key to the body's ability to make and release insulin—declined in both groups during treatment and worsened after treatment ended. An earlier NIH-funded study also found that type 2 diabetes progresses more rapidly in youth than previously reported in adults, despite comparable treatment.

"Only two drugs are currently approved for youth with type 2 diabetes, and we were disheartened to find that neither effectively slows disease progression," said Dr. Ellen Leschek, program director in NIDDK's Division of Diabetes, Endocrinology, and Metabolic Diseases. "Type 2 diabetes in youth has grown with the obesity epidemic, and we need treatments that work for kids. It's clear from this study and others that type 2 diabetes in youth is more aggressive than in adults."

"Our understanding of how type 2 diabetes affects youth is still maturing, and we must continue to explore treatments to ensure that these young people can live long, healthy lives," said NIDDK director Dr. Griffin Rodgers. "These results give us another piece of the puzzle to find which therapies will treat youth with type 2 diabetes."

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

Feedback: In these times of increasing telework and AWS, are there any plans to move staff from off-campus locations (at least for the small ICs)? It would be great if the NIH would find ways to accommodate the extramural staff on campus so that, for instance, staff at Democracy I and II could benefit from the shared resources, instead of the focus on just more parking.

Response from the Office of Research

Facilities: Thank you for your question regarding long-term plans to house extramural staff on the Bethesda campus. The short answer to your question is no. The reasons follow: 1) There is a limited amount of land on the Bethesda campus; 2) There is limited funding in the Buildings & Facilities appropriation with which to fund a new facility; 3) There is a limited amount of parking on campus; 4) There are several leased laboratories that would benefit from being sited on the Bethesda campus; and 5) An independent study conducted by a specialized consultant concluded that, whereas leasing laboratories has proven to be very costly, leasing offices is more affordable.

Given these factors, the long-term strategy approved by the NIH facilities working group (the governance body that oversees the Office of Research Facilities) is to bring locally leased labs back to the Bethesda campus and to continue leasing office space for extramural staff.

NIH recognizes that the geographical separation between the Bethesda campus and the leased offices can create inefficiencies and reduces the opportunities to share resources; however, priority has been given to housing leased laboratories on the Bethesda campus for the reasons cited above.

As an example, thanks to funding via the American Recovery and Reinvestment Act, NIH was able to construct phase 2 of the Porter Neuroscience Research Center, enabling NIH to relocate occupants from 5 Research Court to campus. Similarly, since FDA vacated Bldg. 29B on campus to go to White Oak, NIH is renovating 29B to house, among others, NIAID staff presently located in leased labs in Twinbrook. The synergies, opportunities for collaboration and opportunities to share specialty equipment have proven to be very beneficial to the intramural scientists.

Thanks again for your question. It would be wonderful to house all Bethesda-area staff on the Bethesda campus, but is not feasible at this time.

MILESTONES



NIA's Dr. David Schlessinger in his lab, and with Dr. Luigi Ferrucci, NIA scientific director

Lessons from His First 63 Years in Research: NIA Honors Schlessinger BY CHIP ROSE

The scientific community recently honored the career of Dr. David Schlessinger, an investigator renowned for his achievements in the field of genetics, but even more so as a beloved mentor and colleague.

Schlessinger, senior investigator (now emeritus) in NIA's Laboratory of Genetics and Genomics and NIH distinguished investigator, will start a new chapter in his journey following a recent scientific symposium in his honor at the Biomedical Research Center on the Bayview campus in Baltimore. The celebration included Schlessinger's family and drew colleagues and mentees past and present from NIA, Washington University in St. Louis and other institutions from across the globe.

Schlessinger will be remembered as an expert in the mapping of the X chromosome and the study of its related rare diseases, as well as a noted figure in the history of the human genome effort. Even more, tribute after tribute at the symposium painted a portrait of a respected, beloved and humble mentor and colleague.

Several speakers remarked on Schlessinger's strong support for his mentees, noting his high expectations for everyone, availability to his trainees and the family atmosphere he fostered in his labs. Many speakers also highlighted how he promoted a proper work/fun balance by example, taking his team for the occasional baseball outing (his beloved St. Louis Cardinals or his adopted Baltimore Orioles), incorporating his love for the outdoors by leading nature walks, visiting museums or hosting large potluck meals (with his expert wine selection).

"I enjoyed every minute and every interaction and the many great memories that were recalled."

~DR. DAVID SCHLESSINGER

. . .

He remains an avid traveler, taking in interesting natural sights in the U.S. and across the world with family and colleagues. His travels have often taken them to Italy, home of the SardiNIA project, a large study of aging-related traits in a genetically homogenous population that he has helped lead since 2001.

Schlessinger began his career in fall 1953 at the University of Chicago, where he received his B.S. in chemistry. "The Watson/Crick paper was already in the syllabus for the science courses," he said. "But it didn't have its full impact immediately. At the



Dr. David Schlessinger (5th from left) was celebrated by past mentees Carlos Galaviz, Jose Elias Garcia-Ortiz, Corrado Gurgo, James Chou, Steve Phillips, Weidong Wang, Minoru Ko, Francesco Cucca, Reid Huber and Ramaiah Nagaraja.

PHOTOS: CHIP ROSE, THOMAS WYNN

time the first biochemistry textbooks were being written, a typical statement about DNA would be, 'A boring polymer of repeated units, four repeated units.' So, it took some time for the model to register fully."

While earning his Ph.D. in biochemistry at Harvard University under the supervision of Dr. James Watson, he spent time at the California Institute of Technology, where along the way he met his wife, Alice. They have been married since 1960 and have 2 daughters and 6 grandchildren. Alice is beloved among his mentees for making many international students feel welcome in the U.S. while helping them to improve their conversational English.

Schlessinger later studied at the Pasteur Institut in Paris; he and Alice honeymooned during the ship journey there. "Pasteur was an extraordinary place," he said. "It was a lineup of impressive people, all very original, very interesting. I still think that Paris is the best place in the world to be if you're young. And it's not so bad if you're old!"

Schlessinger went on to make his mark in the field of genetics by leading a Washington University team in the first-ever high-resolution map of the human X chromosome, a feat noted as a "gift to researchers studying X-linked diseases" in the New York Times in 1997. He directed the Center for Genetics in Medicine at Washington University in St. Louis for a decade, leading landmark studies on how the X chromosome related to diseases of aging and human development. He then came to NIA in 1998 as chief of its new Laboratory of Genetics, where he continued to research, publish and mentor.

At the recent symposium, Dr. Luigi Ferrucci, NIA scientific director, recalled how Schlessinger interviewed him for his first position at NIA. "I was nervous because I came from Italy and they were asking very complicated science guestions," said Ferrucci. "But David and I ended up talking about wine and Tuscany, and so I felt instantly at home. He will always be known for his sophisticated science, not just about genetics and aging, but also his way of enjoying aging and life through a variety of experiences and recipes."

For his part, Schlessinger was delighted to reconnect with so many old friends but a bit embarrassed by all the attention. "It was difficult to have so many people that I value arriving to participate and then leaving after such a short time," he said. "But I enjoyed every minute and every interaction and the many great memories that were recalled."

He will retain emeritus status at NIA, and while he has not yet mapped out his full plans for retirement. Schlessinger said they will "certainly include copy-editing manuscripts, which is second nature for me." He also plans to start a memoir of the early days of molecular biology, "written as someone who saw it develop."

Ever a curious mind, he notes that he also has hundreds of books set aside to read now that "I have the time."



Dr. Wendy A. Henderson

NINR Nurse Scientist's Co-Invention Honored with 'Shark Tank' Award

Nurse scientist Dr. Wendy A. Henderson co-invented a new patent-pending methodology to test stool rapidly at the point-of-need for infectious pathogens. The test recently won the 2018 American Gastroenterological Association Tech Summit's Shark Tank competition. Henderson is a clinical investigator and lab chief of the digestive disorders unit within the Division of Intramural Research at the National Institute of Nursing Research.

This first-of-a-kind test is done at the point-of-care and without a laboratory, allowing clinicians to treat patients immediately, since the test results are provided within minutes as opposed to days.

In addition to providing fast results, the paper-based test has the potential to improve outcomes, especially in resource-limited settings in the developing world where 500,000 children a year die from diarrheal diseases.

Henderson developed the tool with Dr. Chang Hee Kim of GoDx under a clinical cooperative research and development agreement, which allows for partnerships between researchers at NIH and private companies. Aspects of Kim's work in this area are also being supported by a Small Business Innovation Research grant funded by the National Center for Advancing Translational Sciences.

NIDDK Alumnus Nikodem Mourned

Dr. Vera Marie Nikodem passed away on May 17 at Sibley Memorial Hospital at the age of 78, after a brief battle with acute myeloid leukemia.

Nikodem was born in 1940 in the former Czechoslovakia during World War II. She graduated from Charles University in Prague in 1962 with degrees in chemistry and biology. She escaped communism and moved to the United States in 1967 to join her



Dr. Vera Marie Nikodem

husband, who was pursuing graduate studies at Princeton University.

Nikodem earned her Ph.D. in biochemistry at Rutgers University in 1975, followed by postdoctoral research at Princeton. She and her family moved to the Washington, D.C., area in 1978 and Nikodem began her 30-year career as a molecular biologist at NIH, culminating as a section chief at NIDDK. During her scientific career, she had a large number of publications and acted as a mentor to many scientists-in-training from dozens of different nations.

Nikodem retired in 2008 and spent her time in both Georgetown and at her second home in Breckenridge, Colo. She was a devoted mother and grandmother, world traveler, gardener and gourmet cook.

Nikodem is survived by her husband of 53 years, Dr. Zdenek Nikodem, sons David and

 $Gregory, daughters\mbox{-}in\mbox{-}law\,Mary\,and\,Bridget\,and\,six\,grandchildren.$

Memorial donations may be made to the Johns Hopkins Kimmel Cancer Center at Sibley Memorial Hospital.

Are You at Risk for Breast Cancer?

NCI is seeking women who are at risk for developing breast cancer. Researchers want to learn more about how certain cells progress to breast cancer. There is one screening visit and one study visit to the Clinical Center to collect cells within the breast ducts. Compensation is provided. More information: Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read about the study at http://go.usa. gov/chSFC. Refer to study 02-C-0077.

Patients with ME/CFS Needed

NINDS researchers are seeking individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) where persistent fatigue started after recovery from an infection. Study participation includes an initial inpatient visit of 5-10 days with up to 8 hours of testing each day. Some participants will be eligible for a second exercise stress study inpatient visit of 5-10 days with up to 8 hours of testing each day and overnight measurement at the Clinical Center. No cost for study-related tests and procedures and you may receive compensation for your participation. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 16-N-0058. Read more at https:// go.usa.gov/xQmWj.

NCCIH Seeks Healthy Volunteers

NCCIH is seeking healthy volunteers 12 and older to participate in a pain perception research study. Compensation is provided. To learn how to participate, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010) or email cc-prpl@cc.nih.gov. Refer to study 16-AT-0077. Read more online at https://go.usa.gov/xQZkr.

Adults with Lung Disease Needed

NHLBI researchers need volunteers at least 18 years old with lung disease to participate in a study looking at how to better measure the effects of lung disease. Study-related tests are provided at no cost and results are shared with you and your doctor. Compensation for travel is provided. Call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://go.usa.gov/xN7NN. Refer to study 96-H-0100.

HIV Vaccine Study Needs Subjects

Vaccine Research Center researchers seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-444-1132 (TTY 1-866-411-1010) or email vaccines@nih.gov. Se habla español.

SEEN

Asian American Pacific Islander Heritage Month Observed

BY ZHONGZHEN NIE AND LAURA WONG

An HHS Asian American Pacific Islander (AAPI) Heritage Month Observance was held May 9 in Wilson Hall. The cross-HHS collaborative effort recognized Asian Americans and Pacific Islanders who have made significant contributions in the federal government.

The event highlighted the 2018 theme "Unite Our Vision by Working Together" with NIH principal deputy director Dr. Lawrence Tabak providing opening remarks. Keynote speaker Dr. Matthew Y.C. Lin, deputy assistant secretary for minority health and director of HHS's Office of Minority Health, inspired attendees by sharing his public health journey and enduring commitment to serve underserved populations around the world.

Plenary speakers included Holly Ham, executive director, White House Initiative on Asian Americans and Pacific Islanders, and Olivia Adrian, president of the Federal Asian Pacific American Council. A panel discussion on Envisioning Careers Toward Science and Public Health, AAPI's Role in Public Service was conducted by HHS AAPI leaders from different agencies.



On hand at the May 9 observance were (from I) Jue Chen, Adelaida Rosario, Josef Rivero, Dr. Matthew Y.C. Lin, Holly Ham, Olivia Adrian, Dr. Eliseo Pérez-Stable, Tyrone Banks, Xinzhi Zhang and Dr. Zhongzhen Nie.

Panelists Dr. M. Chris Langub (CDC), Sally Lee (NIH), Dr. Herb Wong (AHRQ) and Dr. Lei Zhang (FDA) led a discussion with attendees on a variety of topics on career development and effective collaboration. Dr. Eliseo Pérez-Stable, director of the National Institute on Minority Health and Health Disparities, provided closing remarks.

On May 23, the NIH Asian and Pacific Islander American Organization (APAO) organized the 46th Asian American Heritage Month celebration on the Bldg. 31A patio. This year's festivities included a fashion show of traditional clothing from different Asian cultures. Participants were from NIH and the Agency for Healthcare Research and Quality. Students from the Dunhuang Guzheng Academy, an area-based music school, performed on the guzheng (harp) and Arpita Sabud shared a classical Indian dance. In addition, event attendees were encouraged to learn tai chi, Japanese origami and Chinese calligraphy. Eurest Food Services offered Filipino cuisine.

NIH deputy director for intramural research Dr. Michael Gottesman provided opening remarks on the many contributions of Asian American/Pacific Islanders in science and medicine. The PHS Asian Pacific American officers committee, the NIH Employee Assistance Program, NIAMS, the NIH Federal Credit Union and area community groups also participated by providing information tables and displays.

APAO is an independent organization sanctioned by the NIH director's office. It was formed in October 1996 to represent the Asian and Pacific Islander American employees of NIH.



Arpita Sabud performs the Odissi style of traditional Indian dance.



Lonnie Lisle and Jimmy Do wear the Vietnamese ao dai.



Clockwise, from above: The Guzheng ensemble with NIH staffer Ziyi Liu (r). At right, employees of NIH and AHRQ in colorful attire applaud the audience. Edgar Esmaba rocks the Filipino barong with Karen David in Uighur (Central Asia) traditional dress and hat. Wearing Korean han bok are (from I) Youngmi Ji, Minkyung Song and Hyoyoung Choo-Wosoba. Hui Chen writes "NIH" in Chinese characters. Instructors (at right) Hoang-Tam Hilton and Thomas Huppmann teach tai chi basics. PHOTOS: PHILIP BANH, KYAN CHUONG





