ACD Gets Updates on Opioid, ‘Next Gen’ Initiatives
BY CARLA GARNETT

Stopping a current crisis and preventing a future one were just two items that packed the agenda of the 115th meeting of the advisory committee to the NIH director (ACD) on Dec. 14-15. Slowing the nation’s opioid abuse/overdose epidemic and reconfiguring grant funding to reward more innovation earlier in young careers were two of the thorniest topics that the ACD considered at its recent 1½-day session.

In opening remarks, NIH director Dr. Francis Collins put the drug abuse issue in perspective. Noting that all government agencies have been called upon to address the epidemic from all angles, he said that, although no additional research funding has been appropriated for the effort, NIH will do its part to “bring the best science to end the opioid crisis...In the course of the last few years, it’s been getting worse and worse... Now something in the neighborhood of 175 people a day are dying of overdoses—most of those from opioids. More people now are dying per day than at the peak of the AIDS epidemic...We have no justification for anything other than all hands on deck.”

NIDA director Dr. Nora Volkow, who is at the forefront of the NIH Opioid Research Initiative, briefed the ACD on day 2.

“This is the main crisis that we are facing as a nation and what’s disturbing is that we aren’t controlling it and we’re seeing the fatalities go up significantly,” she said.

NIH’s initiative begins with the premise that over-prescription of drugs to manage pain contributed to the crisis, so safer and more effective strategies for pain relief are fundamental to the solution. Additionally, NIH is focusing on two key research areas—innovations to treat opioid addiction and new interventions to prevent and to reverse overdoses.

Volkow reviewed some of the latest science on addiction, including potentially...
NIDCR Symposium Explores ‘Autotherapies’ on Jan. 25

On Thursday, Jan. 25, the National Institute of Dental and Craniofacial Research will convene a scientific symposium “Autotherapies: Enhancing Our Innate Healing Capacity” in Lipsett Amphitheater, Bldg. 10 from 8 a.m. to noon.

Advancing the development of autotherapies is one of the five goals of NIDCR 2030, a vision for the future of dental, oral and craniofacial research. Autotherapies are treatments based on the body’s natural ability to heal and protect itself.

For example, immunotherapy harnesses the body’s immune cells to fight cancer and is now in clinical use. In the dental, oral and craniofacial region, autotherapies could be used to selectively signal the body to repair and regenerate tissue, trigger immune responses and restore a natural microbial balance. These strategies might also help to heal damaged or diseased tissues in other parts of the body, prevent or treat infections, fight cancer, treat autoimmune conditions and enhance overall health.

In opening remarks, NIH principal deputy director Dr. Lawrence Tabak will provide an overview of the topic and goals of the event. The symposium will feature four presentations from experts in stem cell biology, craniofacial anomalies and regeneration, regenerative bioengineering and cancer immunotherapy.

The symposium is free and open to the public; no registration is required. The lecture will be video-cast live and archived. Sign language interpretation is available upon request. Individuals who need accommodation should contact Mary Daum at Mary.Daum@nih.gov or (301) 594-7559.

NIDA Teleconference Discusses Teen Drug Use Survey Results

The National Institute on Drug Abuse hosted a press teleconference Dec. 14 to discuss the findings of the 43rd annual Monitoring the Future (MTF) survey.

This year’s MTF survey of drug use and attitudes among American 8th, 10th and 12th graders in schools nationwide continues to provide encouraging news with self-reported use of alcohol, cigarettes and many illicit drugs remaining at historically low levels.

However, the survey also found that both vaping and marijuana are more popular than cigarettes. And what teens say is in the vaping device varies from nicotine, marijuana or “just flavoring.” The survey also shows continuing decreases in the perceived harms of many drugs, including marijuana.

The MTF survey, funded by NIDA, is conducted by researchers at the University of Michigan. For more on the survey visit https://www.drugabuse.gov/related-topics/trends-statistics/monitoring-future.
FOCUS OF AMD RESEARCH
Microglia Are the Eye’s Electrician

BY KATHRYN DEMOTT

Cells in our eyes called microglia function as a kind of maintenance electrician. They move their fine processes in the retina—the light-sensitive tissue at the back of the eye—constantly assessing the retina’s synaptic connections to make sure they are in good working order. So said Dr. Wai Wong, head of NEI’s unit on neuron-glia interactions in retinal disease, at the 10th Sayer Vision Research Lecture recently.

Since the discovery of microglia as resident macrophage cells of our central nervous system more than 100 years ago, scientists have wondered how they might play a role in neurodegenerative diseases in the brain and the retina. Wong described his team’s work examining how microglia can contribute to the maintenance of a healthy retina, as well as how they go awry during aging and in the context of degeneration.

Specifically, Wong’s research focuses on how microglia contribute to retinal diseases such as age-related macular degeneration (AMD) and retinitis pigmentosa. These diseases are important causes of irreversible blindness in the United States, with multiple forms of these conditions still without effective treatment.

In a healthy retina, microglia contribute to the normal functioning of the connections between nerve cells.

-DR. WAI WONG

In a healthy retina, microglia contribute to the normal functioning of the connections between nerve cells called synapses, Wong explained. The motility of fine microglial processes, as well as their spatial coverage of the retina, enables frequent contact between microglia and synapses, facilitating constant communication and interaction. Evidence shows that microglia actively maintain the function and structural integrity of these connections, enabling the retina’s physiological response to light.

The lab’s studies of mice and primates found that microglial structure and distribution are not static with aging but change progressively. Microglia become more numerous, but individually they are smaller and less branched in structure and demonstrate decreased motility in their processes, suggesting decreasing function with age.

Microglia also change in their response to focal injury as they grow older. Following focal retinal injury, microglia mobilize to the injury site but with aging, they were slower to respond immediately after injury. They also lingered long-term, suggesting that age may predispose them to being part of a maladaptive chronic inflammatory response.

“We also see age-related changes in the distribution of microglia within the retina,” Wong said. In young mice, microglia are confined to the inner retina. As the retina ages, microglia start venturing into the outer retina to accumulate in the sub-retinal space. Studies suggest that microglia in the outer retina become transformed in a way that predisposes the retina to inflammatory diseases.

Wong and his colleagues at NEI are studying the drivers that cause the microglia to age. Understanding those factors may help inform efforts to control or even reverse microglia-related chronic inflammation as a potential treatment strategy for AMD. It’s possible that microglia themselves may become a cellular target for therapy.
significant advances in the area of identifying biomarkers for personalized treatment of opioid use disorder (OUD). She concluded with a 6-item research priority list developed just days prior to the ACD meeting at several large multi-agency, multi-organization meetings:

- Strengthen connection between research and practice
- Explore and use all data sources and study designs
- Engage citizen scientists to help develop metrics for quality of care for OUD treatments, based on reports of actual patient experience
- Determine criteria for inpatient versus outpatient treatment
- Establish most effective treatments for incipient or mild opioid use disorder, which accounts for the largest population in which interventions may have the biggest impact
- Research on costs and sustainability.

Additionally, the NIH public-private partnership to “Address the Opioid Crisis” coordinated by the Foundation for NIH identified two major focus areas—one related to treating opioid addiction and preventing and reversing overdoses; the other towards developing resources and infrastructure to help in the development of potent but safe and non-addictive pain medications.

In an example of the situation’s urgency, Volkow also shared a fast-tracked funding opportunity announcement that NIDA released Dec. 14. The announcement—designed to facilitate creation of partnerships between academicians and the pharmaceutical industry for development of medications to treat or prevent OUD and overdose—remains open through Jan. 25.

Turning toward staving off what could become a future innovation crisis in scientific research, the ACD also learned more about progress on the Next Generation Researchers Initiative (NGRI). “Next Gen” was introduced in spring 2017 to identify novel, measurable ways to restructure the grants process in order to encourage and retain young scientists who are early in their research careers.

“There could hardly be a topic of greater importance if we’re thinking about our future than making sure that we’re providing a pathway for the best and brightest of this next generation,” Collins said. “We need to encourage their vision and [help make their] dreams happen and for science to benefit.”

NIH principal deputy director Dr. Lawrence Tabak, who co-chairs the initiative, described NGRI as “one of the most intensely discussed issues in the scientific community.” He said hundreds of comments from all corners of research flooded his email inbox after Next Gen was announced.

A diverse working group was assembled to tackle a host of concerns, including:

- How NGRI defines the terms “early-stage” and “early-established” investigator
- Determining the correct funding balance for “safe” versus “risky” or “innovative” science
- The research culture’s complex relationship with R01 grants, long considered the top measure of success for a scientist.

In next steps, NGRI will consider monitoring more closely the number of investigators that it funds (not merely the number of grants) and perhaps providing recommendations to prioritize funds, so that investigators who have just missed the payline and are at risk of losing all support are funded.

“At the end of the day, we probably won’t get the perfect solution—in that we’ll get some things for all, but it will not be perfect in terms of expected outcome,” said ACD member Dr. Brendan Lee of Baylor College of Medicine.

Next Gen is a component of the 21st Century Cures Act that Congress passed in 2016. At the ACD meeting a day earlier, Collins had alluded to the importance of nurturing new talent and diversity in research when he talked about lawmakers who had recently come to campus for briefings.

“They’re excited to meet investigators, but when they get the chance to see young scientists in training, they get really excited,” Collins said, referring to members of Congress who tour NIH. “They should—that’s often the best part of the visit.”

ACD member Dr. Elba Serrano of New Mexico State University agreed that making Next Gen a priority is crucial.

“The reason we’re doing this is because Congress got it right,” she emphasized.
“We have to do this for biomedical research to flourish and go into the future. We are working in a system that was developed in the ‘60s and ‘70s and a generation rode that wave into the 21st century, but now we’re in a very different place, a place of team science—possibly the best trained we’ve ever had—and they need their chance to contribute, just like we had ours.”

ACD member and Next Gen working group co-chair Dr. Jose Florez of Massachusetts General Hospital praised the subcommittee’s composition and direction.

“If there’s any doubt in anybody’s mind that diversity’s enriching, [then] I have tangible experience by being on this group,” he noted. “[Hearing from] many different axes really makes a much more rich, productive discussion. In particular the young people who are in the group have been inspirational, thoughtful, articulate, passionate, hard-working and well-informed. Their contribution is particularly valued. I agree with the need to focus on the people rather than grants, expanding the definition of vulnerable at-risk investigators, our desire to make sure that this is a data-driven evidence-based process with scientific rigor...and our desire to not have unintended consequences. The need to continually monitor and evaluate that [NGRI] is having the desired effect is right on target.”


Daily agendas and other meeting documents are also available online at https://acd.od.nih.gov/meetings.html.

Nurse Scientist Describes ‘Giving Voice To the Voiceless’

BY DIANA FINEGOLD, JO-ANN KRIEBEL

When Dr. Mary Beth Happ began her research on improving communication with impaired patients, she couldn’t have known that she would one day find herself using the techniques identified in her research to communicate with a critically ill loved one. However, when a brain tumor limited her own husband’s ability to communicate during his last weeks of life, Happ’s professional and personal lives came together.

Happ discussed this intersection, as well as the research career that led to it, at the third of 2017’s NINR Director’s Lectures in her talk, “Giving Voice to the Voiceless: Improving Communication with Critically Ill Patients.”

Happ’s early research identified the problem of voicelessness in critically ill older adults. These patients were intubated or had preexisting communication disabilities such as poor vision or hearing, which made it difficult for them to express their symptoms and care needs, as well as important end-of-life messages and treatment preferences. According to Happ, nurses for these patients expressed frustration and admitted to avoiding patients for whom communication was most difficult. Thirty years of observational research indicated that there was a need for more tools and training for learning how to best communicate with these patients, leading Happ and her research team to build and test solutions to this problem.

Two such solutions were the Study of Patient-Nurse Effectiveness with Assisted Communication Strategies (SPEACS) and SPEACS-2. Both interventions helped intensive care unit nurses become better trained to work with patients who had communication disabilities and improved the success of communication about pain and other symptoms.

Happ also tested an electronic tablet communication application developed by Dr. Lance Patak, a pediatric anesthesiologist who previously practiced as a critical-care nurse, in a population of mechanically ventilated patients to ensure that the application was easy to use and appropriate for critically ill patients.

Noting that there are still barriers to making tools such as these available in the clinical setting, Happ advocated for broader training in these techniques and for increasing their reach to patients with communication difficulties outside of the ICU.

In her own experience during her husband’s last weeks of life, Happ found making use of the communication tools and techniques she’d studied over the course of her career to be a profound and validating experience. “It kept us connected and reassured him that I was still there and trying.”

Happ is a nursing distinguished professor of critical care research and associate dean of research and innovation at Ohio State University College of Nursing. She is an NIH-funded researcher in the areas of critical care and aging.

The NINR Director’s Lecture Series is designed to bring the nation’s top nurse scientists to NIH to share their work and interests with a trans-disciplinary audience. Happ’s lecture is available on NINR’s YouTube channel at https://www.youtube.com/watch?v=TUG4mDcAXgU.
member of the HHMI-Medical Research Scholars Program]. It was super weird—I didn’t like it.”

Recruited to NCI from directorship of the Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill, Sharpless spent a lively hour Dec. 11 in Masur Auditorium sharing his perspectives on his new job at what he labeled the first town hall meeting of his NCI directorship.

It turns out he is deeply familiar with NIH, is learning more daily as his “listening tour” progresses and has already formed some strong impressions.

“First of all, the research scope of NCI is almost unbelievable—I was truly blown away,” he said. “Each division is like a school of medicine or a school of public health.”

He cited as revelations work in cancer disparities, a major study of the effects of the Chernobyl disaster and collaborations with the Department of Defense and the Veterans Administration.

“The scale of these programs gives NCI the scope to do big things,” he said.

Sharpless is particularly impressed by the MATCH (Molecular Analysis for Therapy Choice) Trial. “This is an audacious effort,” he said, noting that initial data from the 1,100-site trial will be published in 2018. “It will change patient care in the United States and the world.”

He also mentioned the Cancer Moonshot (“a tour de force so far”), a variety of approaches to Ras-mutant cancers emphasizing structural biology and research on cellular and immunologic therapies currently ongoing in Bldg. 10. “This is the only place in the world where this is happening—that’s remarkable.

“Lastly, what most impresses me is the passion and dedication of the people...who are working tirelessly,” said Sharpless, who noted that he has already met hundreds of NCI employees. “O brave new world, that has such people in it. I can’t think of a better job than working with people like you.”

Sharpless said his first scientific job was at NIH, in 1990, as a trainee. “It was the first time I picked up a pipette...I loved that experience. I loved the campus and its intellectual milieu, the stimulating speakers. Within a month of starting, I was telling people it was the best year of my life—up to that point.”

He recalled that as a medical resident, he would sneak off in his free time to read Cell in the library. “I was very interested and passionate about science—I was that guy.”

He admits his research skills atrophied when his clinical duties kept him away from the lab.

“I was very satisfied to treat patients who were sick with cancer,” he recalled, “but when I went back to the lab, I went from being treated like a minor deity on the ward to needing to ask some 18-year-old intern how the tools worked. I felt like an idiot.”

A favorite patient set him on his life’s course. It was a woman in her 40s who, despite grueling treatment and lost hair, was “a very upbeat and wonderful person. She knew she wouldn’t be cured, but her goal was to see her daughter, then age 11, graduate from high school. It was pretty clear that 6 years weren’t possible. But that taught me something. We didn’t have answers for most of our patients. A better understanding of the disease is what we needed most, and I decided I wanted to do that.”

Sharpless had mentors at NCI—Bob Mayer and Bruce Chabner—who assured him that with his passion and talent he’d be successful, despite the inevitable trials of...
navigating peer review and funding uncertainties. “They made me understand that the system does work.”

In 2002, Sharpless opened his first lab, at UNC. His motto? “If you do good stuff, the funding will take care of itself.”

Despite being in Chapel Hill, a place he termed idyllic, for the past 15 years, Sharpless said he’s been “closely tied to NIH my whole career. I’ve been coming to Bethesda a lot, serving on study sections, advisory councils and committees. And I’m an avid reader of science. I felt like I really knew this place.”

While reducing the burden of cancer for patients is his top goal, Sharpless promised “to speak with greater clarity later” about other initiatives he has in mind. He said he is already sure about harnessing Big Data to understand more about treatment and prevention. “We are still not good at telling patients what they really want to know.”

He believes that much useful clinical data is “trapped in doctors’ notes...Free the data! We are shackled by the fact that most of this information is fragmented and disorganized now. We need to learn from everyone’s cancer.”

He said novel devices, therapeutics and diagnostics will be a big emphasis—“I’ve worked on this my entire career.”

And he wants a “full-throated commitment to basic science. There are significant holes in our understanding of the biology of this disease.

“I’m not a big believer in a top-down approach,” he continued. “I believe that the best science bubbles up from smart people following their own curiosity.”

His own basic research on circular RNA grew out of unplanned, unexpected results. Quoting Isaac Asimov, he said, “Scientific discovery starts with ‘That’s funny...’ not with ‘Eureka!’”

He admitted that “making great science happen is like directing lightning where to strike. But we can create an atmosphere where young bright scientists won’t be afraid to try out their crazy ideas.”

Such an atmosphere is supported by stable funding, a macro vision of the mission and reduced bureaucratic hurdles, Sharpless explained.

To prepare for his new job, he sought advice from all living former NCI directors.

“All of them told me that this was a great and wonderful job, and these are great and wonderful people.” They also urged him to take risks.

“NCI can do almost unimaginable things,” he concluded. “I look forward to working with each one of you.”

The hour ended with a Q&A session moderated by Dr. Doug Lowy, who had served as acting NCI director and has returned to his post as institute deputy director. Eleven questions produced further insights:

- Sharpless, who trained as a mouse geneticist, plans to run his own lab in the National Institute on Aging, with a focus on basic cell cycle regulation.

- Sharpless takes the Red Line from his home in Woodley Park (his wife, an endocrinologist, gave up a large practice in North Carolina to come to Washington) and plays pickup basketball Thursday nights at FDA. “I’ve always been an excellent trash-talker,” he disclosed, “if not such a great basketball player.”

- Sharpless believes the Clinical Center, as the crown jewel of U.S. clinical research, “has to be great and awesome in every possible way...but the physical plant is not great and awesome at the moment.” Although he thinks the CC could be more welcoming, its staff—its most important asset—is a problem already solved: “The people are marvelous.”

- Big Data and artificial intelligence must be used to dent the stubborn reality that, in cancer, 25 percent of patients respond to treatment and 75 percent do not. “I can pick up a smartphone and, within seconds, find the best hotels within a hundred miles, but I can’t find the cancer trial that’s best for a patient,” he lamented. “We’re good at calculating the costs of Big Data, but we’re not so good at publicizing the costs of not aggregating data...The molecular genetics of the tumor should drive therapy.”

The session ended on a comic note. Asked by moderator Lowy to name the single overarching message of his incipient NCI directorship, Sharpless paused for effect and said, “What do you think, Doug?”

“More research, and more patients!” answered Lowy, through gales of audience laughter.

Concluded Sharpless, “Basic science is what’s going to do it for us. We’re getting there, and the people who are making it happen are NCI staff.”

The entire session is available for viewing at www.cancer.gov.
Briggs
CONTINUED FROM PAGE 1

Briggs has begun a 6-year term as editor-in-chief of the Journal of the American Society of Nephrology.

“I am very happy for Josie, and I know that she will bring her exceptional scientific and administrative skills to her new position,” said NIH director Dr. Francis Collins. “But I am sad to see her go. She has been an outstanding director, a trusted advisor and a good friend. She is among the most accomplished leaders at the NIH and is universally respected both within and outside our agency.”

“I’m proud of many things as I depart,” Briggs said, “but most of all, I’m proud of the people across this institution who really deliver for the NIH and the American public on extraordinary science. The ability to find such wonderful people, at all levels, and encourage them has been the joy of this job.”

Briggs came to NIH in 1997 to direct NIDDK’s Division of Kidney, Urologic and Hematologic Diseases. In 2006, she left to become a senior scientific officer at the Howard Hughes Medical Institute, but returned in 2008 to direct NCCIH.

“Josie brought a deep understanding of all aspects of research, including translational research, to the center’s studies of complementary health approaches,” said NCCIH acting director Dr. David Shurtleff. “She has had an indispensable role in moving the field forward and expanding the base of rigorous evidence on the safety and effectiveness of these diverse practices and products.”

During her tenure as NCCIH director, Briggs also took on many other large, complex NIH projects. She served as acting director of the Division of Clinical Innovation at NCATS, interim director of All of Us (formerly the NIH Precision Medicine Initiative Cohort Program) and co-chair of the NIH Health Care Systems Research Collaboratory as well as several NIH Roadmap committees. Her memberships included the NIH steering committee (NIH’s most senior governing board), the NIH scientific management review board and the NIH Pain Consortium executive committee.

Being a mentor was another way Briggs shone light: “I am grateful for all Josie did to build an amazing network of young scientists, especially women,” Collins said. “She has lived what some people just talk about. The NIH is an infinitely better place today because of her.”

Briggs’s research interests range from the renin-angiotensin system to science communication. She said of her new job, “I see a journal editor as being in a position similar to a funder. I plan to enhance JASN’s role and focus on publishing the best primary research in the field, from the most basic to the most applied. Chronic kidney disease, in particular, needs a lot more innovative, practical work.”

Briggs received her M.D. from Harvard Medical School and completed her residency in internal medicine and nephrology, and a fellowship in clinical nephrology, at Mount Sinai School of Medicine. She came to NIH from the University of Michigan, where she was a professor of nephrology and physiology.

Her many awards and prizes include the 2014 John P. Peters Award from the American Society of Nephrology for improving the lives of patients and furthering understanding of the kidney, six NIH Director’s Awards, the NIH OD Honor Award, the HHS 2014 Secretary’s Award for Distinguished Service and the Volhard Prize of the German Nephrological Society.

She looks forward to spending time in Maine and D.C. with her husband, Dr. Jurgen Schnermann, retired senior investigator and former chief of NIDDK’s intramural Kidney Disease Branch, and to devoting more time to her family, gardening, drawing, running, biking and other interests. In addition to her JASN job, she will have a position at NCCIH as director emeritus and continue to collaborate with colleagues.

“Josie is proof positive that the impact someone can have at the NIH is completely unrelated to the size of their institute or center,” said NIH principal deputy director Dr. Lawrence Tabak. “Whenever Josie was involved, it made anything better.”

“Whenever Josie was involved, it made anything better.”

-DR. LAWRENCE TABAK

NIDA's Rice Named NAI Fellow

Dr. Kenner Rice of the National Institute on Drug Abuse was recently named a 2017 fellow of the National Academy of Inventors (NAI), the highest professional accolade bestowed to academic inventors who have demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development and welfare of society. The 2017 fellows are named inventors on nearly 6,000 issued U.S. patents. Rice, chief of the drug design and synthesis section, Molecular Targets and Medications Discovery Branch, will be recognized in a January issue of the Chronicle of Higher Education and will be inducted on Apr. 5 at the NAI 7th annual conference to be held in Washington, D.C. He becomes the fourth NAI fellow from NIH.
chemical in *Euphorbia resinifera*, a cactus-like plant pictured above, shows promise for pain relief.

**Chemical from Cactus-Like Plant Shows Promise Controlling Surgical Pain, Study Shows**

A promising approach to post-operative incision-site pain control uses a naturally occurring plant molecule called resiiferatoxin (RTX). RTX is found in *Euphorbia resinifera*, a cactus-like plant native to Morocco that is 500 times more potent than the chemical that produces heat in hot peppers and may help limit the use of opioid medication while in the hospital and during home recovery.

In a paper published online in Anesthesiology, researchers found that RTX could be used to block post-operative incisional pain in an animal model.

Many medical providers turn to opioids, such as morphine or fentanyl, for moderate to severe post-operative pain relief, but these often come with side effects that can interfere with recovery, including respiratory depression, inhibition of gut motility and constipation, nausea and vomiting.

Prolonged use of opioids can produce tolerance and introduces the risk of misuse. RTX is not an opioid and does not act in the brain but rather on the nerve endings in the skin. Scientists found that it can be used to block pain from the surgical incision selectively for approximately 10 days.

In the study, researchers pre-treated the skin incision site with RTX to render the nerve endings in the skin and subcutaneous tissue along the incision path selectively insensitive to pain. Unlike local anesthetics, which block all nerve activity including motor axons, RTX allows many sensations, like touch and vibration, as well as muscle function, to be preserved. Long after the surgery, and towards the end of healing of an incision wound, the nerve endings eventually grow back. Thus, pain from the skin incision is reduced during the recovery period.

**Study Uncovers Clues About Why Common Cancer Drug Causes Hearing Loss**

Scientists have found a new way to explain the hearing loss caused by cisplatin, a powerful drug used to treat many forms of cancer. Using a highly sensitive technique to measure and map cisplatin in mouse and human inner ear tissues, researchers found that forms of cisplatin build up in the inner ear. They also found a region in the inner ear that could be targeted for efforts to prevent hearing loss from cisplatin. The study is published in Nature Communications and was supported by NIDCD.

Cisplatin and similar platinum-based drugs are prescribed for an estimated 10 to 20 percent of all cancer patients. NCI supported research that led to the 1965 discovery of cisplatin and continued development leading to its success as an essential weapon in the battle against cancer. The drugs cause permanent hearing loss in 40 to 80 percent of adult patients and at least half of children who receive the drug.

The new findings help explain why cisplatin is so toxic to the inner ear and why hearing loss gets worse after each treatment, can occur long after treatment and is more severe in children than adults.

“Hearing loss can have a major impact on a person’s life,” said NIDCD director Dr. James F. Battey Jr. “Many adults with hearing loss struggle with social isolation and depression, among other conditions. Children who lose their hearing often have problems with social development and keeping up at school. Helping to preserve hearing in cancer patients who benefit from these drugs would be a major contribution to the quality of their lives.”

Dr. Lisa L. Cunningham of NIDCD led the research team, which included scientists from NIMHD and NCATS.

In most areas of the body, cisplatin is eliminated within days or weeks after treatment, but in the inner ear, the drug remains much longer. Previous research focused on why the inner ear is more sensitive than other parts of the body to cisplatin-induced damage. The NIH team pursued a new angle on the problem: What if the inner ear is not able to get rid of cisplatin and cells in the inner ear important for hearing die because they are exposed to the drug for a long time?

The team developed a mouse model that represents cisplatin-induced hearing loss seen in human patients. By looking at inner ear tissue of mice after the first, second and third cisplatin treatment, researchers saw that cisplatin remained in the mouse inner ear much longer than in most other body tissues and that it builds up with each successive treatment. They also studied inner ear tissue donated by deceased adult patients who had been treated with cisplatin and observed that cisplatin is retained in the inner ear many months or years after treatment.

**Defending Against Environmental Stressors May Shorten Lifespan**

A shorter life may be the price an organism pays for coping with the natural assaults of daily living, according to researchers at NIH and colleagues in Japan. The scientists used fruit flies to examine the relationship between lifespan and signaling proteins that defend the body against environmental stressors, such as bacterial infections and cold temperatures.

Since flies and mammals share some of the same molecular pathways, the work may demonstrate how the environment affects longevity in humans.

Appearing in the *Proceedings of the National Academy of Sciences*, the research identified Methuselah-like receptor-10 (Mthl10), a protein that moderates how flies respond to inflammation. The finding provides evidence for one theory of aging, which suggests longevity depends on a delicate balance between proinflammatory proteins, thought to promote aging, and anti-inflammatory proteins, believed to prolong life. These inflammatory factors are influenced by what an organism experiences in its everyday environment.

Corresponding author Dr. Stephen Shears of NIEHS explained that Mthl10 appears on the surface of insect cells and acts as the binding partner to a signaling molecule known as growth-blocking peptide (GBP).

Once Mthl10 and GBP connect, they initiate the production of proinflammatory proteins, which, in turn, shortens the fly’s life. However, removing the Mthl10 gene makes the flies unable to produce Mthl10 protein and prevents the binding of GBP to cells. As a result, the flies experienced low levels of inflammation and longer lifespans.

“Fruit flies without Mthl10 live up to 25 percent longer,” Shears said. “But, they exhibit higher death rates when exposed to environmental stressors.”

Shears said the research reveals that the ability of a young organism to defend against repeated environmental stress may be an empty victory, because the animal may not live as long. He believes the research may contribute to the discovery of drugs that target excess inflammation induced by signaling proteins in humans, extending life.
NINR Support of Genomic Nursing Described at International Congress

Nurse scientists play a critical role in the health research enterprise, answering questions to improve quality of life for individuals, families and communities. Genomic approaches are becoming increasingly important tools for nurse scientists as they aim to better understand the symptoms of chronic illness.

National Institute of Nursing Research director Dr. Patricia Grady recently highlighted NINR’s support of genomic nursing science in her keynote address at the International Society of Nurses in Genetics 2017 World Congress.

She described the NINR-developed NIH Symptom Science Model, which guides NINR intramural research. Following this model, researchers use genomic and other approaches to develop clinical interventions for complex symptoms.

NINR-supported studies using genomic information include those related to pain and neurological conditions, cancer symptoms, brain injury and peri-natal research.

A significant challenge in genomic nursing science is obtaining data from sufficient numbers of research participants to yield adequate statistical power.

Many large studies may generate extensive symptom-related data, even though symptoms are not the primary focus of the study. “These robust datasets can include genomic, transcriptomic, epigenomic, microbiomic and even clinical data from linked electronic medical records,” Grady noted. Using these existing data sets provides nurse scientists “a wide array of opportunities to address research questions in symptom science.”

To advance the growing importance of “omics” in nursing science, NINIR is developing the Omics Nursing Science & Education Network (ONSEN) in collaboration with NCI and NHGRI. The ONSEN website will be a central resource for those interested in including omics in their program of nursing research. Through ONSEN, nurse scientists will be able to leverage samples and datasets, locate mentors and collaborators and build skills for integrating omics into their research.

In addition to Grady’s keynote, Dr. Lois Tully of NINR’s Division of Extramural Science Programs moderated a panel discussion on the NINR Centers of Excellence program. She also presented a less formal “fireside chat” on research and funding opportunities for nurse scientists.

NINR investigators also presented abstracts on topics including antibiotic use during pregnancy, the effects of blast exposure, ONSEN and genotype-phenotype profiling.
weeks of waiting for the Personnel Support Center to print and mail badges to individuals any time there is a renewal or initial badge issuance.

Taffet played a key role in safeguarding NIH and its workforce. One of his mottos was, “It’s my job to worry.”

Bill Cullen, NIH chief security officer, said, “Those of us who work with Richie, along with his many friends and colleagues, will certainly miss his loquacious wit and dry sense of humor. All of us wish him and his wife Sue fair winds and following seas.”

Nursing Academy Honors NINR’s Gill

Dr. Jessica Gill, Lasker clinical research scholar and chief of the brain injury unit in NINR’s Division of Intramural Research, has been selected as a fellow of the American Academy of Nursing. She was among the 173 nurse leaders honored during AAN’s annual policy conference in Washington, D.C. AAN fellows are nurse leaders who have made significant contributions to nursing and health care. Gill’s research interest is in brain injuries among military personnel, athletes and civilians. More information on her research is available at https://www.ninr.nih.gov/researchandfunding/dir/jgill.

APAO Presents Annual Awards

More than 70 people attended the annual awards ceremony held by the Asian and Pacific Islander American Organization on Dec. 6 in Wilson Hall. Keynote speaker Dr. Janice Lee, clinical director of NIDCR’s Division of Intramural Research, spoke on improved diagnoses through the newest imaging technologies.

In her talk, “Precision Medicine and Personalized Surgery: The Impact on Craniofacial Development,” she described her career path and how awareness of cultural differences in patient populations can enrich physician-patient dynamics.

This year’s APAO honorees include: Dr. Mitchell Ho (NCI) for scientific achievement; Dr. Sudhir Srivastava (NCI) for leadership excellence; and Sara Kaul (NIAID), who received the KT Jeang Distinguished Service Award. APAO also encourages scientists in their early career stages. Two individuals shared the Young Investigator Award—Dr. Haobin Chen (NCI) and Dr. Hien Dang (NCI).

NINDS Alumnus Spector Mourned

Dr. Novera Herbert Spector, who had retired from the Division of Fundamental Neurosciences, NINDS (1978-1995), died on Nov. 15 in Carlsbad, Calif.

He was born on Aug. 23, 1919, in Cincinnati and graduated in 1941 with a biology major from the City College of New York. After working as a machinist, union activist, contractor and scientific instruments salesman, he returned to graduate school to get his Ph.D. in physiology (1967) at the University of Pennsylvania.

His professional appointments included the Medical College of Virginia (1966-1969), University of Lyon (1969-1971), Walter Reed Army Institute of Research (1971-1976), National Science Foundation (1976-1978) and NIH (1978-1995). During his NIH tenure, he remained active in research and graduate teaching with temporary and adjunct appointments at several institutions in the United States and Europe. He maintained his professional contacts and continued writing after his retirement and move to Southern California. A lifelong fencer (U.S. Fencing Hall of Fame and CCNY Athletic Hall of Fame), he started fencing clubs wherever he found himself, including at NIH.

His graduate and early professional research focused on the roles of the central nervous system (especially the hypothalamus) in control loops affecting temperature and body mass regulation and in drug addiction. Starting in the mid-1970s, his research increasingly dealt with the influences of the nervous system on the immune system. He is credited with coining the word “neuroimmunomodulation,” and participated in founding the International Society for Neuroimmunomodulation. He used his NIH position to encourage this then-nascent field of nervous system-immune interactions, for which he received the NIH Director’s Award in 1990.

Flu Vax Study Recruits Healthy Vols

Vaccine Research Center researchers seek healthy volunteers, 18-70 years old, for an investigational influenza vaccine study. Scientists are testing new vaccines to determine whether they are safe and effective in preventing the flu. Compensation is provided. For more information, call 1-866-833-5433 or email vaccines@nih.gov. Read more at https://go.usa.gov/xNH7U. Refer to study VRC316.

Diagnosed with Stomach Cancer?

Have you been diagnosed with stomach cancer? NCI researchers need volunteers 18 or older with stomach cancer that has spread to the abdomen for a study at the Clinical Center combining surgery with heated chemotherapy as a potential new treatment for stomach cancer. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Learn more online at https://go.usa.gov/xXqK. Refer to study 17-C-0070.
Outreach, Education Meeting Strengthens NIAMS Coalition

More than 55 NIAMS Coalition members and 25 NIAMS and other NIH staff met recently for the biennial NIAMS Coalition Outreach and Education Meeting: Creating Connections for Science. Participants received updates from NIAMS and NIH leadership and shared best practices on collaborating with the institute and each other.

NIAMS director Dr. Stephen Katz focused on the three pillars of his institute’s mission: research, training and information dissemination. He stressed the importance of coalition members’ perspectives in NIAMS decisionmaking. “Everything that NIH does belongs to you as patients, researchers, health care providers and as members of the American public,” he said.

NIAMS deputy director Dr. Robert Carter moderated a panel discussion exploring several partnerships that coalition organizations have formed to advance the research enterprise. Panelists Tracy Hart, chief executive officer of the Osteogenesis Imperfecta Foundation; Suzanne Schrandt, director of patient engagement at the Arthritis Foundation; and Dr. Michael Siegel, vice president of research programs at the National Psoriasis Foundation, discussed collaborations they have formed, ranging from grant awards to support for new investigators to educational programs for patients.

Attendees also learned from plenary speakers Eric Dishman, director of the All of Us research program, and Dr. Eliseo Pérez-Stable, director of the National Institute on Minority Health and Health Disparities.

Coalition representatives led sessions on best practices in social media outreach, voluntary organizations and the FDA Patient-Focused Drug Development workshop process, tools and concepts in chronic disease management and implementation of the 21st Century Cures Act. NIH posters offered resources that organizations can share with constituents.

Anita Linde, director of the Office of Science Policy, Planning and Communications, said, “There was great energy in the room as new relationships were being forged and connections were strengthened. We look forward to building on this excitement with our coalition colleagues to further the NIAMS mission in the days and weeks to come.”—Colleen Dundas

Personality Plays a Role in Developing Alcohol Use Disorder

BY ERIN BRYANT

Can personality traits make you more predisposed to problem drinking? Yes, and according to a body of research, personality is an important factor in alcohol use disorder (AUD), which affects an estimated 15 million people in the United States.

Recently, Dr. Kenneth J. Sher, professor of psychological sciences at the University of Missouri, spoke about how and why personality influences the development of AUD during NIAAA’s 22nd annual Mark Keller Honorary Lecture. Sher has been at the forefront of research on the onset and progression of AUD, particularly as it relates to personality traits and their evolution throughout the lifespan.

“There are multiple etiological pathways to alcohol use disorder and personality traits play an important role in most of these pathways,” Sher said. Specific traits have been linked to problem drinking. Among them, negative affect (negative emotions such as sadness, anxiety and anger) is strongly tied to alcohol problems, while traits related to disinhibition, the loss of restraint and inhibition, also seem to play a role. Certain traits are predictive of future problems with alcohol, as well.

“Studies consistently show future alcohol problems are associated with disinhibition/impulsivity and to a lesser degree, neuroticism and negative emotionality,” said Sher. He went on to note that these traits are not unique to AUD, as they are also common to people with anxiety and depressive disorders.

But how exactly does personality affect risk for alcohol problems? Sher discussed several models; one hypothesizes that different personality types have differing sensitivities to alcohol’s rewarding and negative effects. Another suggests that personality influences environmental choices; for example, more extroverted individuals may choose to join a fraternity or sorority, which is associated with excessive drinking.

While personality has been shown to influence drinking behavior, the reverse is also true, with alcohol increasing extroversion while decreasing agreeableness in studies.

Sher explained that drinking problems can also stem from personality change over time. “It was thought that personality is the part of you that doesn’t change—but in fact it changes quite a bit,” he said. Personality is not static and changes over the lifespan affect risk for AUD.

In fact, his work has shown that “maturing out” of problematic drinking is not merely due to the increased responsibilities of adult life—or “role incompatibility” while transitioning to adulthood. His research indicates that lessening of neuroticism and impulsivity over time contribute to aging out of problem drinking.

Ultimately, understanding how personality influences the development of AUD and how these traits evolve over time have clear implications for diagnosis, prevention and treatment.

“The malleability of personality offers a number of potentially novel approaches, both for treatment and prevention,” Sher concluded, noting that this would allow for deeper assessment and personalized interventions.