Ambitious Agenda Engages Advisors to NIH Director

BY CARLA GARNETT

Setting the Precision Medicine Initiative in motion, unveiling the first NIH-wide Strategic Plan in 20-plus years and fine-tuning HIV/AIDS research priorities were just three of the hefty items packing the Dec. 10-11 agenda of the advisory committee to the NIH director (ACD). The group’s 111th meeting convened just a day before the latest temporary federal funding mechanism was due to expire, potentially triggering a government shutdown. However, NIH director Dr. Francis Collins expressed confidence and optimism about NIH’s financial outlook.

“It has been very gratifying for me to see over the course of this entire year the strong bipartisan support for the importance of biomedical research,” he said, opening the ACD meeting, “for the advances that it makes possible in human health, for the way it encourages the economy and for the ways it encourages American competitiveness. The latter is an issue of considerable concern to many members [of Congress].

Almost without exception, this has been a year where, regardless of people’s political views on other matters, the topic of medical research resonated as one that needs to have more attention.

“We’ve gone through a pretty tough time here since 2003—since the end of the doubling, where [grant funding] success rates have continually fallen,” Collins continued, describing his dozens of meetings, briefings and hearings with congressional decision-makers, many of whom have also visited the NIH campus. “This is not a healthy situation for the United States and needs to be attended to...hopefully all of the statements and expressions of goodwill will translate into something we will all be able to celebrate next week.”

[On Dec. 18, President Obama signed into law the FY2016 Omnibus Bill, giving NIH a $2 billion increase in its fiscal year 2016 budget.]

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Fast-Acting Drugs Could Revolutionize Depression Treatment

BY ERIC BOCK

Most antidepressants take weeks to work. Dr. Carlos Zarate hopes to develop one that works within hours. Zarate is senior investigator and chief of the Experimental Therapeutics and Pathophysiology Branch and section on neurobiology and treatment of mood disorders, NIMH. At an Astute Clinician Lecture in Masur Auditorium recently, he reviewed progress in developing the next generation of antidepressants and described

‘BUGS, DRUGS AND STAR TREK’
Jain Explores Future Tools for Infectious Diseases

BY RAYMOND MACDOUGALL

Dr. Sanjay Jain is an avid Star Trek fan who began his recent Wednesday Afternoon Lecture with a nod to the cult TV and film franchise. The quintessential medical device in the starship Enterprise sick bay is the “tricorder”—a hand-held scanner waved over a patient to detect injury and heal all manner of maladies.

“Unfortunately, we don’t have tricorders yet, but we have imaging machines and the concept is pretty straightforward,” he said.

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SEE JAIN, PAGE 8
**Nobel Laureate Kandel Opens ‘Demystifying Medicine’ Series, Jan. 5**

The “Demystifying Medicine” course for 2016 begins on Tuesday, Jan. 5 with a lecture by Dr. Eric Kandel, co-recipient of the 2000 Nobel Prize in physiology or medicine for his research on the physiological basis of memory storage in neurons. The lecture is from 4 to 6 p.m. in Masur Auditorium, Bldg. 10.

Kandel’s talk is titled “The Age of Insight: The Quest to Understand the Unconscious in Art, Mind and Brain from Vienna 1900 to the Present,” based on his most recent book of the same name. He is a professor of biochemistry and biophysics at the College of Physicians and Surgeons at Columbia University, as well as a senior investigator with the Howard Hughes Medical Institute. Kandel trained at NIH in neurobiology in the late 1950s.

Lauded for his scientific contributions, Kandel is also a talented science communicator and popularizer. He chronicled his life and research in the book In Search of Memory: The Emergence of a New Science of Mind, which won the 2006 Los Angeles Times Book Award for Science and Technology. His latest book explores how the interaction of artists, writers, physicians and scientists in the salons of turn-of-the-century Vienna gave birth to a new way of thinking about the mind.

Demystifying Medicine, now in its 12th year at NIH, is directed primarily toward Ph.D. students, trainees, clinicians and program managers. Sponsored jointly by the Foundation for Advanced Education in the Sciences and NIH, the course is designed to help bridge the gap between advances in biology and their application to major human diseases. Each session includes clinical and basic science components presented by NIH staff and invitees.

Course materials are posted at https://demystifyingmedicine.od.nih.gov. Registrants who attend at least 10 sessions and pass a computerized final exam will receive a certificate. All students, fellows and staff are welcome to attend any lecture without participating in the course. For more information, contact course director Dr. Win Arias (arias@mail.nih.gov).

**NIDATalks ‘Monitoring the Future’ Results**

The National Institute on Drug Abuse recently hosted a press teleconference and Twitter chat to discuss the findings of the 41st annual Monitoring the Future (MTF) survey. This year’s survey of drug use and attitudes among American 8th, 10th and 12th graders continued to show encouraging news, with decreasing use of a number of substances, including cigarettes, alcohol, prescription opioid pain relievers and synthetic cannabinoids; and stable rates of marijuana use among teens; and a general decline over the last two decades in the use of illicit drugs.

However, the survey suggested a high rate of daily marijuana use reported among 12th graders—with daily marijuana use exceeding daily tobacco use for the first time in the survey’s history. Additionally, while cigarette smoking rates have declined, rates of use of other tobacco products, including hookah, small cigars and e-cigarettes remain high.

The MTF survey, funded by NIDA, is conducted by researchers at the University of Michigan. For more on the 2015 MTF survey, go to https://www.drugabuse.gov/related-topics/trends-statistics/monitoring-future.

**Interest Group on Biomarkers in Pediatric Therapeutics Forms**

A new biomarkers special interest group in pediatric therapeutics has been established with the primary goal of promoting information exchange and interactions in the application of biomarkers for diagnosis, prognostication, evaluation of disease progression, response to therapy and toxicity in the different pediatric subpopulations. Other goals are to promote initiatives that address knowledge gaps and address issues preventing the implementation of research in this area and to collect and disseminate information related to pediatric biomarkers. In addition, the group will also address pre-clinical biomarkers related to the development of new molecular entities or toxicity evaluation of new drugs tested or developed at NIH.

The first in a series of monthly presentations is scheduled for Tuesday, Jan. 12 at noon in Rockledge II, Rms. 9100/9104. The lecture is titled “Application of Metabolomics To Provide Pediatric Biomarkers,” given by Dr. Susan Sumner, director, NIH Eastern Regional Comprehensive Metabolomics Resource Core, RTI International.

For registration, contact George Giacoia at giacoia@exchange.nih.gov.

**NLM Tours by Appointment Only This Month**

The National Library of Medicine will offer tours of the library by appointment only during January. The decision to temporarily suspend the daily 1:30 tour resulted from an analysis of visitor statistics from the last 5 years. Those interested can book a tour by completing the form at http://infocus.nlm.nih.gov/national-library-of-medicine-tour-request-form/. Groups of five or larger can use this form to arrange a tour for any point during the coming year. The 1-hour tour originates in the NLM Visitor Center, located in the lobby of the Lister Hill Center. Walk-in visitors are welcome to browse the offerings at the NLM Visitor Center weekdays (except federal holidays) between 9 a.m. and 4 p.m. The Visitor Center offers an orientation to NLM through interactive computer displays and print materials.
UMBC Meyerhoff Scholars Visit NIH

BY RAYMOND MACDOUGALL

Undergraduate students from the University of Maryland, Baltimore County, toured bioengineering labs and learned about NIH training opportunities during a recent visit to NIH organized by the National Institute of Biomedical Imaging and Bioengineering’s Division of Interdisciplinary Training. The 14 students are part of the Meyerhoff Scholarship Program, renowned for a 25-year record of advancing diversity among leaders in science and engineering. A high percentage of students in the program go on to earn M.D. and Ph.D. degrees.

NIBIB director Dr. Roderic Pettigrew welcomed the group and reminisced about the lesson that sparked his interest in science at a young age. In his mother’s car, after a class about the Bernoulli principle of aerodynamic lift, wind picked up and tossed papers out the car window. Then, back home, he realized that the vacuum cleaner also demonstrated the principle. “I remember when I was their age and how science held my attention during otherwise turbulent times during the Civil Rights era in the South,” he said. “The Meyerhoff Scholars Program is exceptional at recruiting students who have that spark of interest and supporting their engagement in science and engineering.”

About 300 students attend UMBC as Meyerhoff scholars, according to Keith Harmon, director of the program at UMBC, who accompanied the contingent. About 48 percent of those students study life sciences. “They’re seeing cutting-edge technologies and where the fields are going—things they may not have been exposed to at UMBC or in their summer internships,” he said, during a tour of Bldg. 13’s imaging laboratories. “They are also interacting with professionals and really continuing to develop their own scientific identity, seeing where their training and career options lie for the years ahead.”

Presentations by NIBIB intramural researchers featured super-resolution microscopy of roundworm embryos; an explanation of the biomimetic revolution that has accompanied the discovery of green fluorescent protein from jellyfish and the subsequent development of other photosensitive and photo-activatable spectral probes; an explanation of biochemical principles underlying dynamic protein interactions; and the steps by which imaging is being used to create 3-D models of brain structures.

Senior class member Hilary Bright signed on for the NIH tour as an opportunity to immerse herself in the life sciences. As a biochemistry major, her typical focus is on more technical areas of science. She was fascinated with the use of datasets collected and applied to render 3-D structural models of biological systems. David Reyes Aguilar, in his first year of mechanical engineering studies, encountered “lots of cool stuff” on the tours, which appeals to the biomedical side of his broad interests.

Matthew Shirley, a senior in chemical engineering, has set his goals on earning a Ph.D., but can envision working in a lab like those he was able to visit during the tour. “I am really interested in expanding my knowledge, finding new things out about the world we live in, and I’ve always generally wanted to help people,” he said. “The breadth of resources here at the NIH and the fact that everybody seems really down to earth and interested in their research is definitely a plus.”

Dr. Hannah Valantine, chief officer for scientific workforce diversity at NIH, articulated NIH’s commitment to a diverse scientific workforce and also described her biomedical research into new ways of detecting signals of organ transplantation rejection through her study of circulating, cell-free DNA.

Her talk seemed to resonate with the students, according to Harmon. “Many have an interest in translational research and her illustration of how she’s planning to achieve that was really exciting,” he said. He added that the focus on diversity and on science was a highlight of the NIH visit. “Across the board there was a theme of excellence,” he said. “NIH is about excellence in research, in the workforce, and honoring this idea of diversity of thought and of person. I think that’s very powerful.”

The program also featured a talk by Dr. Darryl Murray, director of the NIH Undergraduate Scholarship Program. He oriented the students to training opportunities at NIH.

The Meyerhoff Scholars Program partners with federal agencies and private organizations. NIBIB has been a program partner since 2005, while the National Institute on Drug Abuse also has participated in supporting the program since 2012. For more about the Meyerhoff Scholarship Program, visit http://meyerhoff.umbc.edu/about/.
some of the challenges remaining in bringing them to market.

Mood disorders such as clinical depression and bipolar disorder are among the leading causes of disability worldwide. Zarate said people with these disorders “have disturbances of mood, behavior, circadian rhythms and activity levels, which cause severe impairment in the ability to function.”

People with bipolar disorder experience depression as well as manic episodes. During the latter, “individuals have increased energy levels, pressured speech, grandiosity, recklessness and significant decrease in the need to sleep,” he said.

Zarate estimated that 40-50 percent of people with major depressive disorder have more than one psychiatric disorder. Up to 90 percent of people with bipolar disorder have more than one psychiatric disorder.

Mood disorders can disrupt a person’s ability to work or attend school and also can damage relationships. They may even cause suicide. Right now, there are 30-40 antidepressants on the market and they may take weeks before they work.

Antidepressants currently available for patients with treatment-resistant depression and bipolar disorder. Zarate said ketamine is an FDA-approved anesthetic used in emergency rooms but not for depression. Its side effects include hallucinations and out-of-body experiences. Best known as an illicit party drug because of its hallucinogenic effects, ketamine is available at off-label clinics in many big cities.

Progress developing new antidepressants has been slow, Zarate said, because of the difficulty in finding suitable models for higher-order brain functions in preclinical studies and also because the brain disorders, by their nature, are extremely complex. Some pharmaceutical companies no longer attempt to develop treatments for brain disorders, he added.

“We haven’t significantly changed the number of suicides that happen each year over time. We have not decreased the prevalence of severe mental illness despite our treatments.”

—DR. CARLOS ZARATE

In several clinical studies, ketamine infusions given intravenously have been shown to relieve symptoms of depression within hours, he said. Symptom relief can last up to a week. Roughly 60 percent of patients responded to treatment.

On average, Zarate said, patients who enrolled in ketamine studies at the Clinical Center have tried at least 7 antidepressants. Most of the patients were unemployed. Half of them had attempted suicide or who have suicidal thoughts. A fast-acting treatment could prevent patients from being institutionalized for lengthy periods of time.

Right now, Zarate is studying the neurobiological changes that occur with ketamine to determine why some patients respond to it and others don’t. He’s observed that patients with a family history of alcoholism are more likely to respond to treatment.

While results are promising, Zarate cautioned that more research needs to be done. It’s not clear what the best frequency of dosing is, although a recent study showed that 2 doses of ketamine in a week is just as effective as 3 doses per week.

Despite the obstacles, Zarate hopes that a drug that mimics ketamine’s antidepressant properties, without significant side effects, could be developed by 2017 or 2018, if all goes well.
Pérez-Stable Addresses Smoking Cessation in Minority Populations

In recognition of National Hispanic Heritage Month, NIMHD director Dr. Eliseo Pérez-Stable spoke on Tobacco Use Behavior and Health Consequences among U.S. Racial/Ethnic Minorities recently in Lipsett Amphitheater.

According to the 2013 National Health Interview Survey, less-educated groups tend to smoke more—those with a GED have the highest smoking rates—and women tend to smoke less than men. For example, 7 percent of Latino women smoke compared with 17.3 percent of Latino men, and 4.8 percent of Asian women smoke compared with 15.1 percent of Asian men.

One study suggests that among Latinos, the association of acculturation and smoking is gender-specific. Latino women who adapt toward English-speaking mainstream society tend to smoke more and pick up other unhealthy behaviors, such as drinking alcohol and eating a poor diet, said Pérez-Stable. Among men, smoking rates decrease and binge drinking behavior decreases with increased acculturation.

In his research, Pérez-Stable found that compared to whites, Latinos are more likely to want to quit because of smoke’s effects on others, especially loved ones and family members, and smoking’s effects on interpersonal relationships and on their own health. Reasons for quitting include criticism from family, their children’s health, wanting to set an example and even eliminating bad breath and holes burned in clothes among smokers. Not gaining weight, however, was not a concern for Latinos compared to their white counterparts.

“The United States has come a long way in reducing tobacco use,” said Pérez-Stable. “It’s not fast enough for some people, but it is progress.”

“Smoking patterns have changed and will continue to change,” said Pérez-Stable. “But the patterns don’t fit with how we have dealt with tobacco use in the last 40 years. We treat smoking as an addiction. Cessation strategies are based on an addiction model. Rather than the exception, very light and non-daily has become the predominant type of smoker.”

Because light smokers are less addicted and non-daily smokers are not addicted by definition, pharmaceutical treatment should be modified for these smokers; behavioral interventions directed at light smokers should be adapted for use in self-help, Internet and quit lines, said Pérez-Stable. No clinical trials have been tested or funded for this type of smoker, he added.

He pointed out that tobacco companies have traditionally targeted youth, women and minority populations, especially African Americans, in order to gain greater market share. Menthol cigarettes, heavily marketed to African Americans, may help explain why this group has a more difficult time quitting, even though they make as many attempts to quit and show the same interest in quitting as whites. Menthol appears to increase smoking dependence by cooling the smoke sensation, but more research is needed, said Pérez-Stable.

In addition, nicotine intake (the addictive chemical found in smoke from tobacco products) per cigarette is 30 percent greater in African Americans, which may explain higher rates (50 percent) of lung cancer in this population. This may also be due to other biological factors and greater metabolic differences than other groups, leading to more intake of carcinogens.

Tobacco affects non-smokers, as well. Second-hand smoke is associated with increased risk of attention deficit hyperactivity disorder among children, cervical cancer and myocardial infarction and exacerbates asthma and chronic obstructive pulmonary disease. Further, in utero second-hand smoke tobacco exposure can affect development of the respiratory tract and is related to persistent asthma in children and adolescents, more emergency room visits and daily and nighttime symptoms such as wheezing, chest tightness, shortness of breath and cough.

To decrease second-hand smoke exposure, indoor smoking bans are effective and have wide health benefits, said Pérez-Stable. Complete smoking bans in households are more common among Latinos and Asians and less common among African Americans.

While minorities tend to smoke fewer cigarettes and less frequently, this has not translated to more smoking cessation success. In order to increase success, clinicians must be persistent in advising patients; greater access to health care is needed; more minorities must be recruited for clinical trials and research studies; and self-help, culturally appropriate interventions should be promoted.

“Clinicians have to play an essential role and we need greater access to health care,” said Pérez-Stable. “It’s not just policies about indoor smoking. We need all of these approaches. Over time, we will see people successful at quitting.”
ACD Meeting
CONTINUED FROM PAGE 1
In a statement, Collins called it “the most encouraging budget outcome in 12 years.”

Following the director’s report, in which Collins highlights what happened at NIH in the 6 months since the last ACD meeting, the group tackled several issues that sparked lively discussion.

The NIH plan to implement the Precision Medicine Initiative Cohort Program topped the ACD’s schedule on day one and a look at innovative research at the National Eye Institute led day two (see sidebars).

Articulating Our Priorities
It had been more than 20 years since NIH attempted the daunting task of putting its broad, trans-institute goals and tactical approaches into a single document. Early in 2015, Collins took up the congressionally mandated challenge to craft an NIH-wide Strategic Plan within a year.

“We took this as a real opportunity to try to articulate what we see as scientific opportunities, how we set priorities and how we think about our role in terms of stewardship,” said Collins. “All of [those considerations] were folded into this plan.”

NIH principal deputy director Dr. Lawrence Tabak was tapped to lead development of the plan, chair the committee of institute and center representatives that hammered out a framework for the document and solicit input on it from various NIH stakeholders both inside and outside the agency. The ACD reviewed a preliminary outline of the plan at its June 2015 meeting; the final was due to Congress on Dec. 16, 2015.

“Truly this has been a team sport,” Tabak said, presenting highlights. “The goal was that the plan should clearly articulate the highest trans-NIH priorities and how we will achieve them. Everyone agreed it needs to be a living document because of the rapidity with which science moves forward.”

[In a Dec. 16 statement, Rep. Andy Harris (R-MD) said, “This groundbreaking NIH-wide strategic plan is an important first step toward increasing accountability and resource prioritization at NIH.”]

New Intramural Component Announced
In mid-May 2015, the Food and Drug Administration held an announced inspection of the Clinical Center pharmacy. Inspectors observed several concerns with

PMI Stands Up, Takes First Steps
The NIH plan to implement the Precision Medicine Initiative Cohort Program drew wide support and applause at the ACD’s Dec. 10 meeting.

Ushering in a “new era of medicine through research, technology and policies,” the Precision Medicine Initiative aims to “empower patients, researchers and providers to work together toward development of individualized treatments.”

The initiative has been on a fast track to fruition since President Obama announced it in his State of the Union address in January 2015.

NIH deputy director for science, outreach and policy Dr. Kathy Hudson, who served as cochair of the ACD’s working group on PMI, tag-teamed with interim cohort program director NCCIH director Dr. Josephine Briggs on a progress report.

Summarizing the working group’s recommendations from September, Hudson pointed out the importance of keeping NIH’s portion of PMI in context with the much broader scope of both the initiative and the global pursuit of precision medicine in general. PMI has two components at NIH—one at NCI and the cohort program. The latter was the focus of discussion at this ACD meeting.

PMI’s initial task, Hudson explained, is to assemble a generational unit, or “cohort,” of one million or more volunteers who reflect the diversity of the U.S., with a strong focus on underrepresented communities. The cohort will be longitudinal, with continuing interactions and opportunities built in for recontacting participants for secondary studies. Initial recruitment of a million participants is estimated to take 3 to 4 years using two methods: direct volunteer enrollment and via partnership with health care provider organizations.

Hudson said a driving issue that planners kept top of mind while devising the PMI cohort was how to maintain participant engagement and enthusiasm over such a long period of time.

“So what are the questions we want to be able to answer and how can we make sure that there is value for the research establishment, for health care providers, for the participants in the cohort and most important for the individual volunteers, early in the short term, in the medium term and in the long term?” Hudson asked, recalling deliberations to develop the cohort. “There’s a whole range of scientific opportunities that cover the waterfront—some that we can realize in the short term and some in the long term that we can’t even imagine today.”

She urged people who are interested in keeping up with cohort progress to use the dedicated web site www.nih.gov/precision-medicine-initiative-cohort-program and to follow #PMINetwork on Twitter.

Explaining the implementation steps already under way, Briggs described how the program will operate, its governance, enrollment targets and early budgetary expectations, announcement of the first funding opportunities and a proposed timeline.

“Translating the [myriad ideas and recommendations for the cohort] into a true, effective plan has been the work of many people,” she pointed out. “What has made the complex project manageable is the relatively high and meticulous level of detail from the working group report. Many key elements were clearly specified…building on the success of the BRAIN Initiative.”

ACD member Dr. Harlan Krumholz of Yale School of Medicine, heartily endorsed PMI’s fledgling steps.

“This is an extraordinary accomplishment,” he said. “There are a couple of revolutionary—not merely evolutionary—things about this that go far beyond the idea of being able to accumulate a million [participants]. One is this commitment to secure data fluidity and access, really going all in on the idea of open science…You are extolling values that will have ripple effects. The example and the principles you’re setting forth from the very outset of this, I believe, are going to have a fundamental impact on the way we see science going forward.”

“The second revolutionary thing,” he continued, “is that you call them ‘participants.’ They’re not ‘patients’ and they’re not ‘subjects.’ The notion of partnership with the people who are going to be involved in this…It took leadership from the top—Francis Collins, I commend you—and it took courage to take this leap” from the traditional structure of medical science wherein scientists conduct the research and consult only each other about the results to this “adaptive, agile model of PMI,” wherein the power and knowledge that stem from science are shared from the beginning with the people.
physical facilities as well as procedures and personnel training. Sterile operations in the CC pharmaceutical development section (PDS) were halted.

By early June, Collins had formed an internal PDS task force cochaired by NIH deputy director for science, outreach and policy Dr. Kathy Hudson and Tabak. External consultants also were engaged for an independent look at the situation. As a result of findings by these groups and meetings with FDA, Collins plans to set up a new quality assurance component, the Office of Research Support and Compliance, within the Office of Intramural Research.

In addition, a new ACD working group on the Clinical Center was formed by the NIH director; a familiar face, Dr. Norman Augustine, will chair the group. A research engineer and retired CEO at Lockheed Martin, Augustine is well-known as a wise advisor to the NIH community, most recently as head of the Scientific Management Review Board. Read Collins’s statement on the PDS at http://1.usa.gov/1IWsSJ2.

### The Ultimate Goal for AIDS: Ending the Epidemic

Many now argue that the scientific opportunity has emerged to eliminate one of the most devastating public health pandemics in the last 35 years: The potential for an “HIV/AIDS-free generation” is within our grasp, according to experts in the field.

As a result, NIH—via its Office of AIDS Research—has taken an aggressive look at its science portfolio on the disease across all components. Beginning with fiscal year 2016, AIDS funding—intramural as well as extramural—will support only research that falls within the highest priorities for the next 3-5 years, said acting OAR director Dr. Robert Eisinger, who presented the portfolio review findings and the four recently honored priorities at the ACD meeting.

“We have come a long way” but HIV/AIDS still poses a significant public health threat, Collins noted. “Our therapies are successful if available, but not perfect. Ultimately we want to move in the direction of achieving a complete eradication of this disease...To get there, this would be a very unfortunate time to take one’s foot off the accelerator. We can see opportunities in such areas as vaccines, and maybe even a cure, that deserve the most intense attention.”

The ACD also received updates from the HeLa working group and NIH’s Big Data effort. Video of gavel-to-gavel ACD proceedings is archived online at videocast.nih.gov.

### NEI Capitalizes on Decade of Remarkable Biology, ‘Audacious Goals’

At the Dec. 11 meeting of the advisory committee to the NIH director, NEI director Dr. Paul Sieving offered “a quick and limited tour” of research at his institute, focusing on two areas—the Audacious Goals Initiative and “some of the interesting breakthroughs that have come out of paying attention to the genetics of eye disease.”

The overarching goal of the 12- to 15-year AGI, he said, is to “regenerate neurons and neural connections in the eye and visual system.” Not only will such an objective have a major impact on a wide variety of eye and vision-related disorders and conditions, Sieving suggested, but also it could shed light more broadly on regeneration in the central nervous system and spinal cord.

“My idea is to accelerate the trajectory of science,” he explained, discussing the origin of AGI. “I value all research, but in this context I value research that will get us to an endpoint of neural regeneration to restore human vision.”

Targeting “bold, inspiring ideas that fundamentally advance vision research and care,” the 2012 AGI Challenge Prize competition brought in nearly 550 submissions; 308 of these came from scientists with no previous NIH grant experience. NEI awarded prizes for the top 10 ideas selected by a federal panel and then used those ideas to shape the audacious goals. NEI announced the first AGI grants, funding research on functional imaging of the visual system, in May 2015.

Sieving also provided ACD members a brief overview of NEI: The institute’s budget for fiscal year 2015 was $677 million. As with most NIH components, the lion’s share—82 percent—was distributed to NEI’s extramural community. About 18 percent to 20 percent of its grant applications were funded. Two-thirds of NEI’s applications were for new projects, with one-third of the new applications coming from new investigators.

NEI’s intramural budget for the same period was $53 million, with 25 lab sections in 5 labs and 50 active clinical protocols.

Sieving pointed out how vision research stacks up when competing with other aspects of neuroscience in general, using the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative as an example.

“THe first BRAIN awards went out in 2014,” he noted, “and vision research did quite well,” garnering 41 percent of awards and 47 percent of the funds. “Because of the organized neural structure of the retina, it is a great place to do discovery on how neural systems are organized.”

Among breakthroughs in the genetics of eye disease cited by Sieving were the use of iPS cells in replacing diseased tissue in the retina and first-ever trials using human stem cells as therapy to treat age-related macular degeneration and Stargardt disease.

“Discoveries of the last decade present remarkable opportunities for vision research,” Sieving concluded. “NEI supports a full spectrum of research, from basic discovery to translational and clinical trials that affect clinical practice...[AGI] puts a spotlight on a place we want to reach.” With concerted effort by scientists from many disciplines, “current momentum promises that we will reach the goal.”

In comments afterward, ACD member Dr. Huda Akil of the Molecular and Behavioral Neuroscience Institute at the University of Michigan said that in her years of experience of talking with investigators in the field, “[It’s from] the people who have been doing the visual research—especially the retinal-related [projects], from year to year, [that] we see the most dramatic progress across different fields of neuroscience. In other areas, you see incremental changes here and there, but the visual stuff is just amazing. The field seems ripe for really transformative [breakthroughs].”

Fellow ACD member and cochair of ACD’s BRAIN work group Dr. Cori Bargmann of Rockefeller University agreed: “The quality of the research and the advances that have happened at the NEI [are] really spectacular. I think that’s partly because smart people like to be with other smart people, and there have been some very smart people specifically in visual neuroscience. I feel like the rest of neuroscience has looked up to them since [1981 Nobelists David] Hubel and [Torsten] Wiesel. But I think it’s also a sign of the leadership at NEI consistently and its support of science and promotion and protection of the best research. You have a very good reputation in the extramural community as an institute that works extremely well with scientists and it’s great to see that at every level, from the molecular to the clinical.”
“You inject a tracer that goes to the bug or whatever metabolic process you want to measure, it’s labeled with something that emits energy, and you have machines that will then tell you where the energy is coming from, which will correlate with the disease process.”

Jain is associate professor of pediatrics and international health at Johns Hopkins University. He also directs JHU’s Center for Infection and Inflammation Imaging Research. He receives support for his work from the National Institute of Biomedical Imaging and Bioengineering, the NIH Common Fund, NHLBI and NIAID. He titled his talk “Bugs, Drugs and Star Trek.”

The technologies that might be needed for tricorder-like medical care may not be light years away, according to Jain. In fact, the Food and Drug Administration has approved three molecular tracers that, with positron emission tomography (PET) imaging, will detect the presence of amyloid plaques in the brains of living patients, a biomarker for Alzheimer’s disease. But he said that there is not a similar tracer yet for infectious diseases. So his team, which investigates how modern imaging methodology can be applied to research on infectious disease and to patient care, has taken up this research challenge.

Jain’s team is conducting experimental work in animals using a combination of computed tomography (CT) and PET scanning techniques to track the behavior of infectious disease in real time. The group’s investigations include imaging studies in tuberculosis, which typically, but not exclusively, attacks the lungs. The laboratory also is developing imaging techniques to detect other bugs, such as the family of bacteria that includes E. coli.

“It is not easy to do imaging for TB because it is a biosafety-level 3 pathogen, which means that it spreads by the aerosol route,” Jain said. To prevent transmission of TB, he devised an air-tight, unbreakable and transparent container to bring infected mice to an imaging facility, accumulating important data to advance understanding of ways to monitor the disease in animals and develop novel bacteria-specific imaging tracers. There are almost 10 million cases of TB worldwide each year, many of which are resistant to drug therapies.

The week prior to his talk, Jain’s group published a case in Lancet Infectious Diseases of a 2-year-old girl who contracted a form of tuberculosis known as XDR TB, or extensively drug-resistant TB. He presented the case as a vignette of the life-and-death circumstances that are a kind of reality check for the work of his laboratory.

The child—now 5 years old and in remission—was seen in the hospital after returning from a 3-month visit to India. She experienced persistent fever, but the doctors’ initial tests could not pinpoint the cause. A chest X-ray revealed a suspicious lung spot, so the doctors tested lung secretions and forged ahead with preemptive treatment for TB. It took 12 weeks for the tests to conclusively identify her case as drug-resistant TB.

With no fast, reliable way to monitor how bacteria responded to the new treatment, the team used CT to rapidly track the response to therapy. The scans were a low-radiation, child-friendly adaptation of that imaging technique, which could become the norm for pediatric CT imaging.

Current imaging methods, such as CT, magnetic resonance imaging and ultrasound, cannot reliably distinguish infection from cancer or other processes. With imaging probes that can specifically label infections, imaging can become clinically useful, Jain said. He presented a variety of promising research studies in which imaging scans with several tracers could detect infections in mice. His lab is hoping to develop a pipeline of imaging probes to identify, locate and monitor a wide range of pathogenic bacteria within laboratory animals and eventually translate those techniques to patients.

Jain emphasized the importance of developing new tools to improve patient care. Contrasting his work with the challenge faced by cancer researchers, who attempt to use imaging to distinguish between healthy and cancerous cells, he says that detecting microbes is relatively easy.

“Microbes—bacteria, prokaryotes and fungi—have had billions of years of evolution and have very unique metabolic pathways and structures,” he said, noting that cell walls in these organisms are completely unique.

“There is nothing like that present in the human body,” he said. “So I think it’s a low-hanging fruit.”

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~DR. SANJAY JAIN

‘Little Stars’ Give CRC Holiday Show

The Zvjezdice Girls Choir, from Zagreb, Republic of Croatia, gave a holiday concert on Dec. 10 in the atrium of the Clinical Research Center. In town for a performance at the Kennedy Center, the choir performed works by Strauss, Britten, Offenbach and Gruber among others. Zvjezdice, or “Little Stars,” Girls Choir is one of the most representative music ensembles in Zagreb. Founded in 1985, the choir consists of outstanding middle and high school students from across the nation’s capital. In three decades of its existence, the choir has worked closely with the most prominent Croatian ensembles and performers, as well as with many conductors from both Croatia and abroad.
Workshop Explores Economics of Prevention

The Precision Medicine Initiative and the Affordable Care Act recognize the value of disease prevention. As NIH expands its efforts in the field, there is growing appreciation of the importance of economic approaches for effectiveness evaluation and intervention design.

To survey recent progress and set future goals, the NIH Health Economics Common Fund Program and the Office of Disease Prevention (ODP) sponsored a recent workshop on economics of prevention.

Participants included directors and deputy directors of NIA, NIMH, NIAMS, ODP and OBSSR and representatives from HHS, CDC and other ICs. Among the speakers were several health economics program grantees. Discussions centered on preventive services utilization, preventive interventions, behavioral economics and intervention evaluation.

In opening remarks, Dr. David Murray, NIH associate director for prevention, emphasized the role of health economics research in advancing NIH’s mission. Dr. Richard Frank, a prominent health economist and current HHS assistant secretary for planning and evaluation, delivered the keynote presentation. He contrasted harms reduction with reduction of use as means of curtailing social costs of tobacco, drugs and other substances.

Dr. Ya-Chen Tina Shih, chief of the section of cancer economics and policy at MD Anderson Cancer Center and a health economics program grantee, analyzed the cost-effectiveness of breast cancer screening in various age groups. Her microsimulation models indicate that broad coverage yields small average gains in health at relatively high cost. Introduction of an effective new breast cancer drug could further reduce mammography’s cost-effectiveness.

Modeling a policy’s consequences is critical to forecasting its impact. Franco Sassi, head of the Organisation for Economic Co-operation and Development Public Health Programme and an NIAAA grantee, urged NIH to invest more in developing shareable models, including those supported by “big data.”

Dr. David Kent, director of predictive analytics and the Comparative Effectiveness Center at Tufts Medical Center and recipient of an NIH health economics award, noted that average results from clinical trials do not reflect individual response variation. Risk-based analysis can help better target preventive interventions.

In the area of behavioral economics, participants noted that small incentives, or “nudges,” can be as effective as large-scale incentives, particularly among low-income groups. Dr. David Laibson, chair of the economics department at Harvard University, discussed the utility of behavioral nudges, such as active choice and default options, for helping individuals act on their intentions for healthy behaviors.

Social factors can provide strong incentives. Dr. Jason Doctor, associate professor at the University of Southern California, reported that the best remedy for the end-of-day rise in inappropriate antibiotic prescriptions is to compare physicians’ prescription rates with peers’ rates.

The meeting concluded with a discussion of future research needs in the economics of prevention led by Dr. John Cawley, professor in the department of policy analysis and management and the department of economics at Cornell University.

A complete meeting summary is available at https://commonfund.nih.gov/healtheconomics/meetings.

OD Celebrates ACEP Graduates

The NIH Office of the Director recently celebrated the graduating class of the Administrative Career Enhancement Program (ACEP). Participants in this inaugural OD staff development program heard remarks from LaVerne Stringfield, associate director for management, OD, and a commencement address from Dr. Richard Wyatt, deputy director, Office of Intramural Research.

Wyatt encouraged graduates to “get out and move around the OD and the ICs, speak to one another, be respectful and civil with those we meet and take responsibility for our own actions. Above all, I suggest we enable and help other NIH’ers to accomplish our NIH mission to ‘enhance health, lengthen life and reduce illness and disability.’”

ACEP was formed to address organizational awareness and professional development for OD employees at the GS-12 level and below. Participants were nominated to the program by supervisors. The program is offered at no cost to staff.

“The support received from leadership throughout the OD was wonderful,” said Sheria Washington, who led the ACEP planning committee.

“My participation in the ACEP was the catalyst to fulfilling my professional aspiration of entering the acquisitions career field,” said graduate Eric Chapman. “The program provided a platform for discussing my career goal with my supervisor and mechanisms for achieving my objective.”

ACEP will continue in 2016. To learn more, contact Washington at sheria@od.nih.gov or (301) 594-8233.
 Boone Heads Loan Repayment Program

BY MANJU SUBRAMANYA

As a college student, Dr. Ericka Boone struggled with the dilemma of taking a summer internship with Merck or one with Penn State’s department of biobehavioral health.

“That decision shaped the rest of my life. I realized this is what I love doing,” said Boone, who studied the effects of alcohol on neurotransmitter systems in the brains of mice that summer at Penn State and went on to get a Ph.D. from the university.

Boone is acutely aware of the quandary young scientists face, debating whether to go into higher paying jobs in private industry and shed their educational debt quickly or follow their passion for research. As new director of the Division of Loan Repayment in the NIH Office of Extramural Research, she is heading a program that can influence their choice.

The Loan Repayment Program (LRP) is focused on attracting qualified physician-scientists to research careers and retaining them by helping pay back up to $35,000 a year for 2 years (total $70K) of their eligible educational debt; awardees are also eligible for 1- or 2-year renewals. The caveat? They must agree to conduct NIH-mission relevant research for 20 hours a week at a domestic nonprofit or government agency over the same period.

“Doing research comes at a sacrifice,” noted Boone, who was a postdoc at Emory University and the University of Illinois. “I had friends who bought houses and had great careers, while I drove a Ford Escort for 14 years.

“We want to remove the financial burden and get the message out about the program, as the LRPs represent an important investment by NIH in the future of health discovery.”

“Congress saw indebtedness of physician-scientists, including dentists and veterinarians, as one of the major barriers that forced them from research into direct clinical care,” said Dr. Sherry Mills, director of the Office of Extramural Programs at OER and Boone’s supervisor.

The LRP, mandated by Congress, funds some 1,500 researchers a year outside of NIH, with annual awards totaling $65 million to $70 million (see https://www.lrp.nih.gov/). “We are taking bright physician-scientists, eliminating most of their educational debt, helping them stay in research and starting their trajectory into independent research.” Mills said.

Mills praised Boone as “very smart, very focused and someone who has embraced the spirit of the program in a core way. She carries the best interests of participants at all times and is a super advocate for applicants and staff.”

Boone joined NIH in 2008, working in NIDA’s Office of Science Policy and Communications, where she developed publications on substance use and abuse. She later began assisting with the LRP at NIDA, becoming an LRP program officer in 2010 and NIDA’s LRP liaison in 2013. When the LRP division director job opened up at OER, it seemed an ideal fit for her qualifications. Boone applied and was named director recently.

The daughter of a Navy officer, Ernest Kimbrough, and a Department of Transportation contractor, Toni Kimbrough, Boone grew up in a big family (four sisters and a brother) and moved around a lot. The Virginia Beach native says she gets her joy for life from her father and her “knuckle-down, hard work ethic” from her mother.

In her spare time, she makes jewelry, travels and loves attending jazz, R&B and gospel concerts.

A single parent, Boone says she has been absorbed for the past 18 years in raising her son, Evan, a college freshman. She has volunteered at his school since his pre-K days and is currently a volunteer on the NAACP Parents’ Council in Montgomery County.

And she has graduated to a Hyundai Sonata.

Lisanby To Direct NIMH Division of Translational Research

Dr. Sarah Hollingsworth Lisanby has joined NIMH as director of the Division of Translational Research (DTR). She comes from Duke University School of Medicine, where she was chair of the department of psychiatry and behavioral sciences and J.P. Gibbons professor of psychiatry. Prior to that, she was chief of the division for brain stimulation and neuromodulation at Columbia University/New York State Psychiatric Institute and professor of clinical psychiatry at Columbia.

Lisanby is a leading researcher in the area of neuromodulatory interventions for treating major depression. She has received numerous awards for her research, including the Max Hamilton Memorial Prize of the International College of Neuropsychopharmacology, the Klerman Prize from what is now the Brain & Behavior Research Foundation and the Eva King Killam Research Award from the American College of Neuropsychopharmacology.

In addition to research, Lisanby has served on numerous advisory panels, editorial boards and professional associations. She has served as president of the Association for Convulsive Therapy (now the International Society of ECT and Neurostimulation) and the International Society for Transcranial Stimulation and as chair of the American Psychiatric Association task force to revise the practice of electroconvulsive therapy (ECT).

As DTR director, Lisanby will oversee a research funding portfolio of about $400 million and help set a national agenda for research on mental illness.

“Doing research comes at a sacrifice. I had friends who bought houses and had great careers, while I drove a Ford Escort for 14 years.”

- DR. ERICKA BOONE
Medical Arts’ Brown Mourned

Linda Brown, 73, who worked for the Medical Arts Branch for over 48 years and was an integral part of the branch’s creative process and culture, died Oct. 25 after battling cancer for 3 years.

In January 2014, Brown retired from her role as creative services director, which she held for 17 years. But she returned immediately as a volunteer and mentor, exemplifying her dedication to NIH and the creative process. She also volunteered at the NIH history office, helping with the archives of years of illustrations, posters and photographs created by Medical Arts staff. Brown admitted that she could not picture herself not working, so she slowly transitioned into retirement. She concluded her volunteer work at the end of 2014.

Brown considered herself old-school and believed that whatever she produced should be quality-driven. When she transitioned from being an illustrator to creative services director, she was still able to keep some important projects for herself. In the latter role, one of her responsibilities was to interview Medical Arts’ clients and match them to the best team to get the job done. “I like to play matchmaker,” she said. “I managed the more complicated projects,” organizing the tasks and workloads.

Brown could tell which designer or illustrator completed a project simply by looking at it. She was able to distinguish her employees’ artwork by the type of ink used, inconspicuous signature designs or particular techniques.

“With tremendous creative energy, Linda worked to create a vision and an award-winning NIH standard of art as it applies to communicating discoveries in biomedical research,” said Tammie Edwards, Medical Arts chief. “She ensured the continuation of this tradition by training and mentoring numerous creative staff over the years, including myself. We have always considered her a national treasure.”

Survivors include a sister, Mary Ann Marmon, nieces Karen Marmon and Nancy Carson, nephew Glenn Marmon and granddaughters Rachel and Leah Rosenberg, as well as many close friends.

In remembrance of Brown and her dedicated efforts, Medical Arts is planning an art show to celebrate her life’s works and contributions, date pending.

Liver Disease Patients Needed

An NIDDK research team seeks people with fatty liver disease to participate in a study. Researchers are looking at a breath test to measure how the body breaks down food in people with fatty liver disease. If you have been diagnosed with non-alcoholic fatty liver disease or steatohepatitis, you may be interested in participating. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 15-DK-0080.

Volunteers Needed for Energy Study

NIDDK seeks healthy Caucasian females, 18-35 years old, to participate in a research study. Doctors want to learn how the body burns energy at different temperatures. You will have an 8-day inpatient stay at the Clinical Center. Compensation is provided. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Refer to study 12-DK-0097.

Become a Healthy Volunteer

An NIH research study is enrolling healthy persons ages 18 to 65 who are free of psychiatric disorders and certain medical conditions. Researchers will evaluate the effects of the experimental medication ketamine on brain receptors in healthy and depressed adults. Study includes 1 to 6 weeks of outpatient procedures: a screening visit, computer tasks, rating scales, neuropsychological testing, two intravenous infusions, a blood draw, brain scans (MEG & fMRI) and may include optional 2-4 overnight stays for a sleep study. The study is conducted at the Clinical Center. There is no cost to participate and compensation is provided. To find out if you qualify, email moodresearch@mail.nih.gov or call 1-877-MIND-NIH (1-877-646-3644), TTY 1-866-411-1010. Refer to study 04-M-0222.

Students Visit NIH to Explore Science Careers

Fifteen students supported by the NIGMS Institutional Development Award (IDeA) and Native American Research Centers for Health (NARCH) programs recently took part in a week-long enrichment opportunity at NIH. The program, now in its third year, was developed by NIGMS and the NIH Office of Intramural Training and Education (OITE) to expose American Indian, Alaska Native and Native Hawaiian students to biomedical research and related careers.

The IDeA program builds research capacity in states that historically have had low levels of NIH funding by supporting basic, clinical and translational research, faculty development and infrastructure improvements.

NARCH supports research, research training and faculty and infrastructure development through partnerships between American Indian/Alaska Native tribes or tribally based organizations and research-intensive academic institutions.

The students, who ranged from undergraduate to graduate level, came from all over the country to participate in science career workshops, networking seminars and hands-on lab activities.

Jody Shimabukuro, a graduate student at Hawaii Pacific University, said she was inspired by her meetings with NIH staff.

“Not only have I grown professionally and personally, but this visit has solidified my commitment to science,” she said. “I’m already thinking of coming back to NIH for an internship.”—Chidinma Okparanta

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With the sort of delicacy one associates with patient arrivals, gingerbread houses were delivered to the front door of the Clinical Center on the morning of Dec. 7, which was the start of NIH’s 12th annual Gingerbread House Decorating Contest. Several creations were borne lovingly on wheeled aluminum gurneys, some of which were carried, to prevent vibrations from damaging the houses (see above). Bearing precious cargo are (from l) Sarah Puryear (postbac), Nadeene Riddick (IRTA), Ellen White (postbac) and fellows Fan Wu and Kenta Matsuda of NIAID’s Laboratory of Molecular Microbiology in Bldg. 4. Their house (right) features many Minions. Visitors to the display were invited to vote for their favorite houses, either by paper ballot or on Facebook. The Foundation for the National Institutes of Health donated the gingerbread house kits. From there, imaginations soared. At left, from top, are some winners: 1st place, paper; 1st place Facebook, 3rd place paper; and 3rd place Facebook. For all winning entries, visit Seen online at https://nihrecord.nih.gov/newsletters/2016/01_01_2016/seen.htm.

The Maryland School of Dance spread holiday cheer to pediatric patient families on Dec. 13 by performing excerpts from The Nutcracker at the Children’s Inn at NIH. The concert was sponsored by The XA Project, a non-profit charity founded by Dr. Audie Atienza. He is a health scientist at NIH who created the organization to bring the joy and beauty of the arts to children facing serious medical conditions.

The Clinical Center hosted a Horn Quartet performance by National Symphony Orchestra members (from l) Scott Fearing, Chandra Cervantes, James Nickel and Abel Pereira on Dec. 8. The group performed a selection of holiday music. The event, cosponsored by the Foundation for Advanced Education in the Sciences, represents the National Symphony Orchestra’s 13th visit to NIH as part of the NSO Sound Health initiative, which brings orchestral music to area hospitals and medical centers.