**THERAPIES FORESEEN**

**Bakaletz Shows How to Bust a Biofilm**

BY RICH MCMANUS

It was while Dr. Lauren Bakaletz and her team were trying to create a vaccine for otitis media—the middle-ear infection familiar to most new parents and a significant cause of deafness in the developing world—that they happened upon the technology to disrupt biofilms.

What are biofilms, you ask? They are not movies shown to high school sophomores during science class, but crafty little living blankets prone to setting up residence on any surface, such as the bones of the middle ear (a biotic surface) or on the metallic surface of your newly replaced hip joint (abiotic surface).

Brawnier than blankets, though, biofilms act as a kind of shield, protecting bacteria embedded within them. “Resident bacteria in a biofilm are typically 1,000-fold more resistant to antibiotics than their free-living counterparts,” Bakaletz said.

“[Biofilm-associated infections] are very common, they are very complex and they are very difficult to treat,” said Bakaletz, professor of pediatrics and otolaryngology, vice president for basic sciences and director of the Center for Microbial Pathogenesis at the Research Institute at Nationwide Children’s Hospital in Columbus, Ohio. She gave the Wednesday Afternoon Lecture recently in Masur Auditorium.

“Any device put in the body is prone to biofilm development,” she continued. Biofilms are also associated with sinusitis, chronic urinary tract infection and wound infections.

Bakaletz has spent her entire career studying otitis media (OM), an ailment that typically recruits commensal bacteria found in a person’s nasopharynx. Worldwide, there are 709 million new OM cases yearly, with 21,000 deaths, usually due to meningitis. There are more than

**Scientists Must Replicate Findings, Ioannidis Says**

BY ERIC BOCK

Science isn’t perfect. But, it’s still one of the best things to happen to humankind. However, researchers must strive to improve the robustness, efficiency and transparency of their studies, said Dr. John Ioannidis at the Robert S. Gordon, Jr. Lecture in Epidemiology held recently in Masur Auditorium.

“We need to find out how we can best perform, communicate, verify, evaluate and

**THE POWER OF THINKING**

**Learn How to Become a Resilient Leader, Shatté Advises**

BY DANA TALESNIK

Sometimes we’re our own worst enemy, focusing on the negative, feeling overly frustrated or anxious, projecting defeat. It’s an outlook that can lead to depression and burnout. One antidote is resilience, a competency and a mindset that sets us up for success.

“How we think is the most powerful
Webinar on Global Burden of Disease Study, May 7

The Office of Disease Prevention will hold a webinar on the Global Burden of Disease Study: Quantifying Health Loss to Inform Health Policy. It will take place on Tuesday, May 7, at 12:30 p.m. Dr. Stephen Lim will summarize the history, analytical principles and methods underlying the Global Burden of Disease Study. He will describe the work and results of a collaboration with ODP to estimate disease burden for the population under 70 years of age.

Lim is professor of health metrics sciences and senior director of science and engineering at the Institute for Health Metrics and Evaluation at the University of Washington.

To register visit https://prevention.nih.gov/global-burden-disease-gbd-study-quantifying-health-loss-inform-health-policy. The webinar will be recorded and available on the ODP website within about a week.

NIH Career Symposium, May 10

The NIH Office of Intramural Training & Education invites all NIH graduate students and postdoctoral trainees, both basic scientists and clinicians, to participate in the 12th annual NIH Career Symposium on Friday, May 10 at Natcher Conference Center from 8:30 a.m. to 5 p.m. The symposium provides an opportunity for fellows and graduate students to learn about scientific career options and to explore factors that lead to career success. The program will include more than 20 breakout sessions highlighting career opportunities.

Panel sessions cover academic, government, industry and non-profit career paths. More than 80 speakers will provide insights into their careers. For more information and registration visit https://www.training.nih.gov/.

Pride Month Events Planned for June

NIH will celebrate June as Pride Month with an awards program for SGM community members and a speaker on June 20.

Sexual and gender minority (SGM) is an umbrella term that encompasses lesbian, gay, bisexual and transgender populations as well as those whose sexual orientation, gender identity and expressions or reproductive development varies from traditional, societal, cultural or physiological norms. This includes disorders or differences of sex development (DSD), sometimes known as intersex.

Award nominations are sought for individuals who help advance SGM research or help make NIH a more welcoming environment for individuals in SGM communities. The award is open to all NIH employees and fellows.

Nominations should be made by Friday, May 17 to https://www.edi.nih.gov/people/sep/lgbti/pride-2018/nominations. Include the nominee’s name, title and email address, say how the nominee addresses issues in the SGM community and specify whether the nominee is a member of the SGM community.

Awardees, who must be NIH employees, will be honored during the first annual EDI Sexual & Gender Minority Community and Ally Leader Awards ceremony at the event “PRIDE in the Diversity of NIH” on June 20 at Natcher Conference Center, balcony C from 2 to 3:30 p.m. Guest speaker will be Dr. Sharon Milgram, director of NIH’s Office of Intramural Training & Education.

For all inquiries, contact Bali White at (301) 594-0155 or bali.white@nih.gov.

Celebrate Public Service Recognition Week, May 5-11

Each year the President and Congress designate the first full week of May as Public Service Recognition Week (PSRW) to honor government employees.

Spread the word about NIH during Public Service Recognition Week and show your NIH pride. Tell why you serve by participating in NIH’s PSRW social media campaign. Follow these guidelines:

- Take a photo with your completed “I Heart Public Service” whiteboard template (found at https://hr.nih.gov/about/events/psrw).
- Post photo on Facebook, Twitter or Instagram using the following: #NIH, #PSRW and #Proud2ServeUSA. The NIH hashtag allows viewers to find NIH employees.
- You can also send your photo to NIHPSRW@nih.gov. Images will be posted on NIH social media outlets.

Another way to share in the spirit of PSRW is by thanking others for their service. Give a colleague a Public Service Star Award for his/her great work. A printable template of the Star Award can be found on https://hr.nih.gov/about/events/psrw.

To learn more about PSRW festivities happening around the region, visit https://psrw.ourpublicservice.org/. If you have any questions about PSRW at NIH, email NIHPSRW@nih.gov.
Tromberg Touts Computational Modeling at Meeting

BY RAYMOND MACDOUGALL

How can mathematical models that are developed on computers and in laboratories be translated for decisionmaking in the clinic and operating room, or for government policies and disseminated to experimental researchers and K-12 students? Federal program officers and federally supported researchers in computational modeling addressed this question at the Interagency Modeling and Analysis Group (IMAG) 2019 Multiscale Modeling Consortium annual meeting, a 2-day event held at NIH recently.

The 12th annual meeting focused on translation and dissemination of models and had more than 500 attendees in person and watching online.

The consortium—nearly 400 investigators who conduct modeling and analysis of biomedical, biological and behavioral systems—partners with IMAG, composed of more than 100 program officers from more than 10 agencies of the federal government who promote this research. Their joint efforts are represented in the more than 100 modeling and computational analysis projects underway in federally supported laboratories.

NIBIB director Dr. Bruce Tromberg, in his first official talk to a workshop at NIH since arriving in January, conveyed great enthusiasm for the opportunities surrounding multiscale modeling and computation in biomedical sciences.

“As many of you who are developing technologies know, it’s important to commercialize and disseminate,” he said. “This is a wonderful opportunity to get something that works and get it into the hands of lots of people.”

His research, prior to taking the helm of NIBIB, has entailed multiscale imaging and technology development—from macroscopic, to microscopic, to molecular imaging. He envisions opportunities, working with modelers, to predict outcomes for patients.

He explained the potential of bioimaging combined with measurement to detect physical properties of tissue, including composition, perfusion, metabolism, structural features, cell sizes and the size and density of scattering particles. “All of these things are absolutely model-dependent,” he said.

Tromberg told the audience that his most widely cited scientific article, published in 1994 and now having 1,300 citations, turns out to have been a paper in which modeling and computation underpinned an important imaging framework.

He reasoned, however, that models must then be converted into instrumentation and technologies. In one example, his work has been applied to develop an optical technique that can detect tumor tissue in the breast and help predict the patient’s response to therapy.

Now, at NIBIB, Tromberg believes that modeling and data science are an essential tool driving innovation in technologies to advance synthetic biology, development of point-of-care, wearable and implantable devices, imaging instrumentation and therapeutic tools and systems. He also has already been tapped to co-chair the strategic planning committee for the NIH Data Science Initiative, where he sees an opportunity to apply computational modeling.

“There is going to be broader, more widespread access to these established, multiscale NIH datasets that are enormously valuable and will drive remarkable research and discovery,” he said.

“This is going to accelerate the development of new analytical tools and standards for the modeling community.”

On hand at the meeting were (from l) IMAG chair Dr. Grace Peng, NIBIB; meeting keynote speaker Dr. Charles Taylor of HeartFlow, Inc., and Stanford University, who develops computer modeling and imaging techniques for cardiovascular disease research, device design and treatment planning; and meeting co-chair Dr. Jeffrey Holmes of the University of Virginia.
Biofilms
CONTINUED FROM PAGE 1

330 million cases annually of chronic suppurative OM (CSOM), resulting in some 50,000 deaths, usually to children under age 5. CSOM is associated with more than 50 percent of hearing loss worldwide, with disease burden mostly borne by those in developing countries.

As moms and dads everywhere know, antibiotics—“pink medicine”—are the most common treatment for OM, but prolonged use of antibiotics gives rise to antibiotic-resistant strains of bacteria, compounding an already significant public health problem.

Biofilms are behind both OM and otorrhea, the drainage exiting an infected person’s ear, Bakaletz said. And behind the persistence of biofilms is the EPS—extracellular polymeric substance, or matrix—that surrounds and supports the bacteria within a biofilm. It is a kind of armor protecting the bugs that make us sick.

The gold standard for studying OM in animals is the chinchilla. The bony septae within the animal’s ears provide a natural depth gauge for measuring deposits of the hardy, pulpy white substance that proves so difficult to clear with antibiotics.

It is the mucosa of the middle ear upon which these living films take up residence and play their role in the recurrence and chronicity of OM.

Bakaletz and her colleagues took a deep dive into the matrices and bacteria that form biofilms and found that they are characterized by an abundance of extracellular DNA (eDNA) and associated DNA-binding proteins (especially DNABII). They found “a tremendous lattice of cross-hatched DNA,” indicating that biofilms enthroned and protect the bacteria upon which they form. DNABII “serve as linchpins of the lattice, to stabilize eDNA,” she said.

The researchers found similar lattices in wounds forming after cesarean section and from the sputum of children with cystic fibrosis.

They wondered: Could anti-DNABII antibodies collapse the lattice, thereby resolving the infection?

Studies employing that strategy revealed a reduction of more than 86 percent in the thickness and biomass of the biofilm in vitro.

Further, Bakaletz believes the technology developed by her team can disrupt many biofilms, not just those created by nontypeable Haemophilus influenzae, the bacterium at the root of chronic and recurrent childhood cases of OM.

An ancillary benefit of inducing lattice-collapse is that standard antibiotics suddenly work more robustly than ever, with 4 to 8 times better efficiency, Bakaletz reported. Stripped of the protection of the matrix, free bacteria are more easily eliminated.

“So we can use [antibiotics] at a lower dose” when they are applied synergistically with the collapse-inducing antibodies.

Also intriguing is that only 8 to 12 percent of the bacterial cells within a population were releasing the eDNA and DNABII proteins targeted by anti-DNABII antibo.

ies, yet aiming at this target was “enough for a cure.”

Bakaletz and her collaborators, encouraged by early success in developing a therapeutic immunization regimen in chinchillas, now believe they can spur the development of antibodies that can resolve other human diseases, not just OM.

Their painstaking work developing chimeric peptide immunogens targeting the tips and tails of bacterial cells has revealed that anti-tip chimeric Fab fragments are the most effective therapeutic in their studies, to date.

“What is the human response to these proteins?” she wondered, noting that this is important to know as part of her team’s assessment of them for use in clinical trials. One OM trial envisions transcutaneous vaccine delivery via a kind of band-aid placed behind the ear.

Funded for her entire career by the National Institute on Deafness and Other Communication Disorders, Bakaletz concluded, “I hope there is a clinical use for our observations.”

During a brief Q&A, she noted that cystic fibrosis is among the diseases short-listed for future trials employing DNABII-targeted therapy. She predicts benefits will likely extend to implanted medical devices, as well as to animals, including pets and livestock.

NIDA Helps Out at Baltimore Science Fair

Members of NIDA’s diversity and outreach committee represented the institute recently at the Baltimore Science Fair at Towson University.

More than 100 middle and high school students participated in the fair, presenting their work to judges from FDA, NIH, the U.S. military, the National Security Agency and Johns Hopkins University, among other organizations. NIDA staff awarded prizes to nine young scientists.

Serving as judges were: Miguel Arenivar, Scientific Director’s Fellowship for Diversity in Research (SDFDR) fellow and postbac in the Yeka Aponte lab; Francisco Battiti, SDFDR fellow, postbac in the Amy Newman lab; Dr. Brenton Laing, postdoc in the Aponte lab; Kathy Lightfoot; Dr. Hanbing Lu; Adrianna Hayden, postbac in the Aponte lab; Adam Moreno-Mendelson, SDFDR fellow, postbac in the David Epstein lab; Maria Ortiz, SDFDR fellow, postbac in the Antonello Bonci lab; Leslie Premo; and Dr. Michelle Jobes.

For more information and photos of the science fair, including the awards ceremony, visit www.baltimoresciencefair.org.
Symposium Marks ‘All of Us’ Anniversary
On Monday, May 6, the All of Us Research Program commemorates the one-year anniversary of the program's launch with a symposium—From Data to Discoveries: Creating a Research Program for All of Us—in Masur Auditorium, Bldg. 10, from 10 to 11:30 a.m. The symposium will look at what it has learned so far about building an engaged and diverse participant community and its potential for scientific impact.

All of Us is a historic, longitudinal effort to gather data from one million or more people living in the United States to accelerate research and improve health. By considering individual differences in lifestyle, socioeconomics, environment and biology, researchers will uncover paths toward delivering precision medicine—or individualized prevention, treatment and care—for all of us.

When the program launched on May 6 last year, it was in a style and scope unprecedented for NIH programs. At seven launch events across the country, speakers such as Veronica Robinson, the great-granddaughter of Henrietta Lacks, and Illinois Sen. Dick Durbin were simulcast and livestreamed for a broad viewing audience. Grassroots educational fairs went on at places such as the 50-yard line at Detroit's Ford Field, in the pews of Abyssinian Baptist Church in Harlem and at Cloud Gate in Chicago’s Millennium Park.

In the year that followed, All of Us traveling exhibits visited such places as the Hailey Public Library in Hailey, Idaho, and the annual Zonta Arts & Crafts Festival in Pascagoula, Miss., to spread the word across the country. From Birmingham, Ala., to Pasco, Wash., more than 215,000 registered individuals (as of Apr. 15) of diverse professional backgrounds, genders, ages and sexual orientations have enrolled with the common goal of advancing precision medicine.

The symposium this year will examine the building blocks of creating a meaningful research program that engages a diverse participant community. Speakers including NIH director Dr. Francis Collins and National Institute on Drug Abuse director Dr. Nora Volkow will discuss the cohort’s and dataset's potential to affect scientific research.

All of Us Director Eric Dishman will acknowledge the successes the program has already realized and discuss the need for continued commitments. Lightning talks by several of the program’s consortium members will cover the critical need for diversity and inclusion in research, the science of engagement, data as a tool for empowerment and how technology can advance research.

Researchers can also learn about the interactive data browser tool, the first of several products for researchers that the program will deliver this year as part of the All of Us Research Hub. The data browser will offer details about participant data using information collected through surveys, electronic health records and physical measurements. A Data Snapshots page will provide a curated set of summary statistics about the All of Us participant community and data.

Khoury, Pittman Lectures Featured at Masur in May
The NIH Director’s Wednesday Afternoon Lecture Series (WALS) will host the annual George Khoury Lecture on May 8 and the annual Margaret Pittman Lecture on May 15.

The Khoury Lecture will be presented by Dr. Julie Pfeiffer, professor of medicine at the University of Texas Southwestern Medical Center. Her talk is titled, “Getting by with a little help from their friends: how bacteria aid virus infection.” Her laboratory is studying several areas related to RNA viruses, pathogenesis, viral evolution, viral population dynamics, host barriers and the effect of intestinal microbiota on enteric viruses. The lab’s overall goal is to understand virus-host interactions that affect the development of disease.

This lecture was organized by NIH scientists to honor the memory of Khoury, who was highly regarded as a superb scientist and caring mentor of the postdoctoral fellows in his laboratory.

The Pittman Lecture will be presented by Dr. Lucile Adams-Campbell, professor of oncology at Georgetown University Medical Center. Her talk is titled, “A community approach to breast cancer prevention: addressing health disparities.” Adams-Campbell’s research addresses health disparities with a particular emphasis on cancers that disproportionately affect African-Americans. Her research focuses on lifestyle interventions including physical activity, energy balance, obesity, metabolic syndrome and oral health among minority and underserved populations.

The Pittman Lecture is given by a researcher dedicated to advancing and improving the careers of women scientists. Since 1994 when this annual lecture began, every speaker has exemplified the intelligence, scientific excellence and drive that made Pittman a leader as the first female laboratory chief at NIH.

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

Participate in OBSSR Crowdsource
The Office of Behavioral and Social Sciences Research is seeking comment and input from the research and health/public health communities to help inform a list of public health and health care accomplishments/contributions resulting from behavioral and social sciences research. OBSSR has launched a public comment platform at https://obssr.ideascale.com/ to engage the research community for the development of a broad accomplishments list. The deadline to participate is July 31. For inquiries or more information, contact OBSSRnews@mail.nih.gov.

NIDA Director Receives Two Awards
Dr. Nora Volkow, director of the National Institute on Drug Abuse, is the recent recipient of two scientific awards. At left, on Apr. 5, she received the Presidential Award from the American Society of Addiction Medicine during its 50th annual conference in Orlando. The award, presented by ASAM president Dr. Kelly J. Clark (r), honors individuals for “outstanding dedication and service in addressing addiction issues or promoting education, training or awareness of the specialty of addiction medicine.” Volkow also received the “Keeper of the Flame” award from the American College of Academic Addiction Medicine for being an advocate of ADM’s mission “to build a trained workforce of ADM physician specialists to serve as clinical experts, faculty, researchers and system change agents.”
We need to find opportunities to change the way we do science in our everyday environment.”

-DR. JOHN IOANNIDIS

When too many basic scientific findings are essentially wrong, the results will “lead people astray” and waste resources downstream, said Ioannidis.

PHOTOS: MARLEEN VAN DEN NESTE

Reproducibility can be grouped into three clusters, Ioannidis noted. One is reproducibility of methods, which means “to repeat exactly as possible the experiment and computational procedures.” Next is reproducibility of results, which means “we’re doing another study on new participants, samples and observations and we hope to get a result that is consistent, compatible—ideally as close as the original.” The final one is “reproducibility of inference,” which means scientists ask others about their conclusions. They may disagree about what the results mean.

Attitudes toward replication have changed over the past decade. Ioannidis says industry has led the change in preclinical research because they spent millions of dollars on experiments that led nowhere. Several companies launched reproducibility checks on highly cited papers published from top academic institutions. They found most of the results could not be reproduced.

Although reproducibility efforts are becoming more accepted, they can be “tricky” and “emotional” because investigators of the original work might fiercely challenge the results, with their careers and reputations at stake.

Millions of scientists write research papers. Ioannidis believes they must register their studies, unless they are admitted to be exploratory. Openness would also improve the chances that other scientists can see if the research holds up. Studies should also disclose any conflicts of interests, to become more transparent.

There has also been progress in sharing data since 2015. Before then, it was rarely done. Several medical journals, for instance, have changed their policies to encourage data-sharing. More work must be done to create a culture in which researchers freely share their data, said Ioannidis.

“We need to find opportunities to change the way we do science in our everyday environment,” he concluded.
Germaine Louis, summing up her experience learning to explain each bend in her career path as a strength, not a detour.

“[Equally] important are my roles as daughter, niece, friend, colleague, wife, mother and grandmother, as they ground my career and keep me righted as a researcher,” she said.

In her talk, “A Winding Path to a Rewarding Career in Public Health,” Louis emphasized the strengths of a nonlinear career trajectory. She followed a childhood dream and trained and worked as a registered nurse at Millard Fillmore Hospital in Buffalo, N.Y., where she was first exposed to public health. She promptly fell in love with the field. Studying reproductive epidemiology in graduate school at the State University of New York at Buffalo, Louis was discouraged by the scarcity of training grants available to students interested in the subject. She continued to work as a nurse to support herself and her family.

In 2000, Louis was invited to be a senior investigator and chief of the Epidemiology Branch at the National Institute of Child Health and Human Development. She recalled that it was easy to say yes to the job. “Doing risky, impactful work that can’t be done on the grant mechanism—it was really seducing to somebody like me.”

She also recognized that the position would enable her to encourage initiatives that highlight public health research. “It would be an opportunity and Perinatal Epidemiological Research and the Canadian Institute for Health Research, she laid out a plan to enhance reproductive and perinatal epidemiology through training grants and a summer institute, respectively. Louis went on to co-edit a textbook on reproductive and perinatal epidemiology that stemmed from the summer institute’s curriculum.

Today, Louis calls upon all her previous work experiences as a nurse, professor and researcher in her role as dean at George Mason University. She said that these varied life experiences give her a stronger, more interdisciplinary approach, which in turn, makes her a better leader, professor and mentor.

The symposium addressed institutional barriers hindering women from pursuing science careers and examined policies, practices and strategies that have been effective in opening doors to women in the sciences. Dr. Donna Shalala, former HHS secretary and current U.S. congresswoman representing Florida’s 27th district, delivered the keynote address. She chaired the NAS committee that issued the seminal report Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering.

Dr. Vivian Pinn, first full-time director of ORWH, introduced Shalala.

ORWH director Dr. Janine Clayton participated in a panel on scientific agencies and foundations designed to improve women’s representation in the sciences.

The event also informed an ongoing NASEM consensus study chaired by Dr. Mae Jemison, former NASA astronaut and the first African-American woman to travel into space. The study, due in the spring of 2020, will examine data on why women are underrepresented in the sciences, help institutions understand how to remove barriers that impede women in scientific careers and recommend evidence-based practices and strategies to improve representation of women in scientific disciplines, particularly in leadership roles.

Resilience

CONTINUED FROM PAGE 1

predictor of how resilient we’re going to be,” said Dr. Andrew Shatté, author and research professor, University of Arizona School of Medicine. “More than any other factor—more than education, experience or training—it’s resilience that determines who succeeds and who fails.”

Shatté, who also is founder and president of the consulting and training firm Mindflex, LLC, delivered a motivational, entertaining lecture recently to a packed Masur Auditorium as part of the Deputy Director for Management seminar series.

Resilience is a trait we admire in people who have gone through great change or adversity or who have persisted toward achieving major feats. It arises in trailblazers who didn’t lose hope, who kept trying until they finally solved a problem, got an invention to work or won the race.

Shatté has devoted much of his career to developing programs that encourage resilience in children, college students and the corporate workforce. Over the last 13 years, he also has studied resilience in the federal government. His surveys show that federal employees are typically more resilient, with higher job satisfaction, than their private sector counterparts, though optimism has waned recently due to fiscal cliffs and furloughs.

Anyone can learn to become more resilient, said Shatté. It takes perseverance, optimism and flexibility. It also takes empathy, which helps us strengthen the meaningful relationships and networks that can sustain us through hard times.

Another key ingredient is learning to keep emotions in check. Getting too emotional, he said, interferes with goals and erodes resilience.

To illustrate his point, Shatté engaged the audience in a word-jumble activity. He posted a series of anagrams, asking the audience to try to unscramble the words. Afterward, he asked who felt frustrated, anxious, angry or embarrassed going through the exercise because, it turned out, only one of the words was solvable. The exercise, he said, was intended to demonstrate the power of thinking style: when we have setbacks, we can choose to languish or to resilience by recalibrating our minds so they’re focusing on the positive.

“These emotion radars rob us of our emotion regulation, which is a critical piece of the resilience puzzle,” said Shatté.

In one psychology study, noted Shatté, undergraduates were given hundreds of unsolvable anagrams following by a simple puzzle. Nearly two-thirds of the students, despondent from the previous anagram exercise, could not solve the easy puzzle.

Recognize defeatist thoughts early, said Shatté. “Once they get out of our heads and we’re looking at them more objectively, as scientists should, then we can recognize them for what they are: a perception based on habit and not an index of who we are.”

Studies among children have shown the benefits of learning to stay calm under pressure. In the NIMH-funded Penn Resilience Program, begun in the early 1990s, findings from more than 30 controlled trials involving hundreds of thousands of children showed that building resilience by conquering their thinking styles made kids more resistant to depression.

One gauge of resilience is a person’s “why style,” said Shatté. Do we blame others and the circumstances, or do we blame ourselves in the moment, realizing there are variables we can change to improve the outcome?

For example, asking why a child is failing math could produce a range of answers such as: I’m terrible at math; the exam was too hard; the teacher hates me; or I didn’t study hard enough. The last answer, said Shatté, shows the greatest flexibility. The “it’s me, but not always, not every time” mentality reduces the propensity for depression, workplace impairment, absenteeism and the likelihood of quitting.

Positivity improves productivity and reduces chronic stress, said Shatté, yet our brains seem hardwired toward the negative.

“We don’t savor the positive to the same degree that we live and experience the negative,” said Shatté. “We try to advocate for people to rebuild and refresh their resilience by recalibrating their minds so they’re focusing on the positive.”

When work matters, when people feel they’re contributing to something larger than themselves, as so many federal employees do, this breeds resilience.

“More than any other factor—more than education, experience or training—it’s resilience that determines who succeeds and who fails.”

-DR. ANDREW SHATTÉ

“When we become more resilient,” said Shatté, “we can challenge the thinking that leads us to fail and take opportunities and challenges that come our way...I do believe the most significant wellspring of resilience is a life of meaning, mission and purpose.”

Shatté then rattled off a long list of NIH research accomplishments, after which he noted that the examples were just some of what’s been achieved in the last 5 years. He also said NIH’s numbers in federal employee surveys were quite high in such variables as emotion regulation and empathy but, similar to other federal employees, a little lower on optimism.

“It reflects the fact that we can maintain a sense of resilience under great stress and pressure if we’re doing something for the right reasons,” said Shatté. “Hold on to this sense of meaning because it is everything.”
NIMHD Hosts Commonwealth Fund Fellows

BY JULIET C. PEÑA

The future of minority health and health disparities relies, in part, on physician leaders who promote policies and practices to improve care for underrepresented and disadvantaged populations.

The Commonwealth Fund Fellowship Program in Minority Health Policy, supported by the National Institute on Minority Health and Health Disparities and the Commonwealth Fund, is helping to develop such leaders. Fellows complete a year-long intensive study in health policy, public health and management while earning a master’s in public health or public administration. They also participate in leadership forums and seminars to help advance health care delivery.

NIMHD recently welcomed the five physicians from the 2018-2019 Commonwealth Fellowship Program in Minority Health Policy at Harvard University. The fellows, all engaged in various areas of minority health research, gathered at the Democracy II Bldg. to learn more about ongoing programs at NIMHD and other NIH organizations, where they could gain further experience in the field.

Dr. Carl V. Hill, director of NIA’s Office of Special Populations, shared research opportunities in minority health and health disparities. He mentioned Alzheimer’s disease as a major area of NIA research in minority groups, including disability populations and sexual and gender minorities.

In order to ensure a well-rounded analysis, “our researchers look at potential pathways of disease at multiple levels,” he said. “That includes environmental, sociocultural and behavioral analyses.” Hill suggested using an NIMHD-NIA-supported resource, the Neighborhood Atlas, to gain insight on these underlying factors at the community level.

NIMHD director Dr. Eliseo Pérez-Stable offered important reminders. “Minority health is not always about minority groups doing worse,” he said. “We also research in the areas where they excel, such as resilience and life expectancy” with regard to Latinas.

Pérez-Stable also highlighted upcoming updates in the 2020 classifications of race and ethnicity by the Office of Management and Budget. For example, one new category will include the Middle Eastern/North African group. In addition, African Americans, like Latinos, will have the option to indicate their country of origin. Further classifying racial/ethnic subgroups may help researchers understand the mechanisms behind different treatment responses.

“It is important to know how similar we are as well as how different we are,” said Dr. Larissa Avilés-Santa, director of clinical and health services research at NIMHD.

Dr. Marion Kosso-Thomas, a medical officer at NICHD, talked about women’s and children’s health research programs and rationales behind them. For instance, with the Global Network, “We want research to be cost-effective and to use something that makes sense in that area,” she said.

One NICHD-supported project helps women prepare before they get pregnant, with nutritional interventions for mothers-to-be to prevent low birthweight.

In addition, NICHD is working toward developing a maternal and newborn health registry to see if low-dose aspirin reduces pregnancy complications or preterm labor.

“Health registries can inform policymakers,” said Kosso-Thomas. “Making informed guidelines and engaging with communities are essential. Community engagement is really about engaging the people. No white coats.”

Dr. M. Constanza Camargo, an Earl Stadtman investigator at NCI, shared global research efforts in reducing gastric cancer disparities.

“We are 100 research investigators in the Intramural Research Program [at NCI],” she said, pointing out significant gender and racial disparities in gastric disease linked to an individual’s environment, diet and genes. Camargo’s team and collaborators in Chile are trying to help reduce these disparities in various ways, including identifying biomarkers to predict disease risk.

“We are trying to collect more data to help health care providers make decisions,” she said.

Dr. Karen L. Parker, director of the Sexual and Gender Minority Research Office (SGMRO), discussed the NIH Sexual, Gender and Minority Research Strategic Plan for FY 2016-2020, which marked an agency-wide attempt to engage all institutes and centers.

“We didn’t want this research to be siloed,” she said. “Our expectation is that, when appropriate, all research ICs think about coordinating.” Currently supporting more than 370 studies, SGMRO anticipates funding more projects each year. In 2019, the office will host regional workshops at Emory University and Thomas Jefferson University.

With many research opportunities presented, the Commonwealth Fund fellows and NIH presenters discussed potential collaborations on existing and future projects in minority health and health disparities.

Bike to Work Day Set

On Friday, May 17, Commuter Connections and the Washington Area Bicyclist Association invite you to celebrate bicycling as a clean, fun and healthy way to get to work. Be one of the first 20,000 to register and attend this free event, then bike to your choice of 115 pit stops in D.C., Maryland and Virginia and receive a free T-shirt, refreshments and be entered into a raffle for a new bicycle.

For registration information, visit https://www.biketoworkmetrodc.org/.

AGA Honors NINR’s Henderson

Dr. Wendy A. Henderson, chief of the digestive disorders unit in NINR’s Biobehavioral Branch, has been selected to participate in the American Gastroenterological Association (AGA) Future Leaders Program. She joins 17 other early-career physicians and scientists who were selected for this competitive program based on their current achievements, dedication to advancing the field and potential for future success. Henderson is the first nurse scientist to be selected to this program. “With the AGA Future Leaders Program, we are developing a healthy pipeline of future leaders who will guide AGA for years to come in its mission of empowering clinicians and researchers to improve digestive health,” said Dr. Darrell Pardi, co-program chair.

“We look forward to working with these rising stars and preparing them for continued success and achievements in gastroenterology.”
Gene Therapy Restores Immunity in Infants with Rare Disease

A small clinical trial has shown that gene therapy can safely correct the immune systems of infants newly diagnosed with a rare, life-threatening inherited disorder in which infection-fighting immune cells do not develop or function normally. Eight infants with the disorder, called X-linked severe combined immunodeficiency (X-SCID), received an experimental gene therapy co-developed by NIH scientists. They experienced substantial improvements in immune system function and were growing normally up to 2 years after treatment. The new approach appears safer and more effective than previously tested gene-therapy strategies for X-SCID.

Infants with X-SCID, caused by mutations in the IL2RG gene, are highly susceptible to severe infections. If untreated, the disease is fatal, usually within the first year or two of life. Infants with X-SCID typically are treated with transplants of blood-forming stem cells, ideally from a genetically matched sibling. However, fewer than 20 percent of infants with the disease have such a donor. Those without a matched sibling typically receive transplants from a parent or other donor, which are lifesaving, but often only partially restore immunity.

“A diagnosis of X-linked severe combined immunodeficiency can be traumatic for families,” said NIAID director Dr. Anthony Fauci. “These exciting new results suggest that gene therapy may be an effective treatment option for infants with this extremely serious condition, particularly those who lack an optimal donor for stem cell transplant. This advance offers them the hope of developing a wholly functional immune system and the chance to live a full, healthy life.”

New Tool May Transform Study of Brain Structure, Function

Researchers have developed a high-tech support system that can keep a large mammalian brain from rapidly decomposing in the hours after death, enabling study of certain molecular and cellular functions. With funding through the BRAIN Initiative, researchers developed a way to deliver an artificial blood supply to the isolated postmortem brain of a pig, preventing the degradation that would otherwise destroy many cellular and molecular functions and render it unsuitable for study. Importantly, although the researchers saw some preservation of flow through blood vessels and energy use, there was no higher level functional activity in the brain circuits. The scientific team, led by Dr. Nenad Sestan of Yale University, reported their findings Apr. 17 in the journal Nature.

“This line of research could lead to a whole new way of studying the postmortem brain,” said Dr. Andrea Beckel-Mitchener, BRAIN Initiative team lead at NIMH, which co-funded the research.

“The new technology opens up opportunities to examine complex cell and circuit connections and functions that are lost when specimens are preserved in other ways. It also could stimulate research to develop interventions that promote brain recovery after loss of brain blood flow, such as during a heart attack.”

Researchers’ ability to study the functional dynamics of an intact, isolated large postmortem brain has been hampered by cell death, clotting of small blood vessels and other toxic processes that degrade the tissue following loss of blood flow and oxygen. Freezing and other preservation methods allow for only static microscopic, biochemical or structural analyses.

To overcome these limitations, Sestan and colleagues created a system called BrainEx (after “ex vivo”), specially designed to attenuate some of the processes responsible for degradation of tissue in postmortem brains. The researchers used brains from a pork processing plant that would have otherwise been discarded. The system involves pumping a solution called BEx perfusate—a proprietary mixture of protective, stabilizing and contrast agents that act as substitutes for blood—into the isolated brain’s main arteries at normal body temperature.

Brains processed with BEx showed reduced cell death, preserved anatomical and cell architecture, restored blood vessel structure and circulatory function, restored glial inflammatory responses, spontaneous neural activity at synapses and active cerebral metabolism, compared to brains perfused with a control solution, which rapidly decomposed. Importantly, there was no global electrical activity that would indicate higher-order functions, such as awareness or perception.

The results suggest that delivering protective agents to the brain through its dense network of blood vessels may hold potential for improving survival and reducing neurological deficits after trauma.

Want To Learn a New Skill? Take Some Short Breaks

In a study of healthy volunteers, NIH researchers found that our brains may solidify the memories of new skills just practiced a few seconds earlier by taking a short rest. The results highlight the critically important role rest may play in learning.

*Everyone thinks you need to ‘practice, practice, practice’ when learning something new. Instead, we found that resting, early and often, may be just as critical to learning as practice,” said Dr. Leonardo Cohen, NINDS senior investigator and a senior author of the paper published Mar. 28 in the journal Current Biology. “Our ultimate hope is that the results of our experiments will help patients recover from the paralyzing effects caused by strokes and other neurological injuries by informing the strategies they use to ‘relearn’ lost skills.”

The study was led by Dr. Marlene Bönstrup, a postdoctoral fellow in Cohen’s lab. Like many scientists, she held the general belief that our brains needed long periods of rest, such as a good night’s sleep, to strengthen the memories formed while practicing a newly learned skill. But after looking at brain waves recorded from healthy volunteers in learning and memory experiments at the Clinical Center, she started to question the idea.

The waves were recorded from right-handed volunteers with a highly sensitive scanning technique called magnetoencephalography. The subjects sat in a chair facing a computer screen and under a cone-shaped brain-scanning cap. The experiment began when they were shown a series of numbers on a screen and asked to type the numbers as many times as possible with their left hands for 10 seconds, take a 10-second break and then repeat this trial cycle of alternating practice and rest 35 more times. This strategy is typically used to reduce any complications that could arise from fatigue or other factors.

As expected, the volunteers’ speed at which they correctly typed the numbers improved dramatically during the first few trials and then leveled off around the 11th cycle. When Bönstrup looked at the volunteers’ brain waves, she observed something interesting.

“I noticed that participants’ brain waves seemed to change much more during the rest periods than during the typing sessions,” she said. “This gave me the idea to look much more closely for when learning was actually happening. Was it during practice or rest?”

By reanalyzing the data, she and her colleagues made two key findings. First, they found that the volunteers’ performance improved primarily during the short rests and not during typing. The improvements made during the rest periods added up to the overall gains the volunteers made that day. Moreover, these gains were much greater than the ones seen after the volunteers returned the next day to try again, suggesting that the early breaks played as critical a role in learning as the practicing itself.
Hagan Retires from NIGMS

After more than three decades of service to NIH, Dr. Ann Hagan retired on Mar. 31 as NIGMS’s associate director for extramural activities. At NIGMS, Hagan earned the moniker “problem solver in chief” for her remarkable ability to balance rules with common sense.

Along with serving as executive secretary to NIGMS’s advisory council, Hagan provided valuable guidance to staff and grantees. She recommended many improvements in day-to-day processes, such as shortening review times, recognizing new and early-career investigators and establishing guidelines for continuing operations in crisis situations.

Hagan is also noted for her tireless support of coworkers. Dr. Susan Gregurick, director of NIGMS’s Division of Biophysics, Biomedical Technology, and Computational Biosciences, said, “I consider her a mentor and a friend. She met with me every month and provided invaluable guidance and assistance in understanding how NIGMS advisory council, grant processes and NIGMS policies and processes work.

“She was always open, and she was the first one to step up and help with a difficult problem,” Gregurick added.

Dr. Laura Moen, former NIGMS scientific review officer and now director of the Division of Extramural Research Activities at NHLBI, noted that Hagan was “patient with those of us who were still learning—anything to make NIGMS, and NIH, a better place.”

Hagan earned a Ph.D. in physiology from the University of Illinois and came to NIH in 1979 as a visiting scientist. She joined NIH in 1987 as an extramural grants review branch. In 1989, she became a scientific review administrator at NIDDK and moved up the ranks until she was chief of her branch. In 2000, she came to NIGMS as deputy director for extramural activities.

Hagan says she’s looking forward to pursuing other passions now that she has the time. By retiring in the spring, she’ll finally be able to put in the garden she always wanted, yielding lots of produce that may embellish new recipes. She notes, too, that Duke, her canine family member, will be especially delighted to have her around the house more in the coming weeks.

NIBIB’s Krosnick Mourned

Dr. Steven H. Krosnick, director of the NIBIB program in image-guided interventions and head of the NIBIB Portfolio Evaluation Office, died on Apr. 1 following a battle with cancer. During a 20-year career as an NIH medical officer, Krosnick’s prior positions included program director in NCI’s Division of Cancer Treatment and Diagnosis and scientific review administrator in the Center for Scientific Review.

Krosnick spent his childhood in Bucks County, Pa., and graduated in 1979 from Pennsby High School. He received his bachelor’s degree from the University of Pennsylvania in 1983 and his M.D. from Tufts University School of Medicine in 1987. He continued training in the Tufts University system for diagnostic radiology and radiation oncology, with board certification in both.

During Krosnick’s 8-year leadership of the NIBIB program in image-guided interventions, he cultivated a portfolio of projects encompassing cutting-edge technologies for imaging and robotics to enable less-invasive and more accurate surgeries. These have included techniques to perform minimally invasive intracranial surgery, real-time intra-operative MRI guidance during brain tumor surgery, illumination of nerves during surgery and image-based guidance for spine surgery.

Expressing the loss felt by colleagues at the institute, NIBIB director Dr. Bruce Tromberg said, “Steve was a widely admired and generous colleague who cared deeply about his coworkers and the NIH community.”

Krosnick is survived by his wife Lisa, daughters Rebecca and Sarah, mother Selma and sister Phyllis Lavine.

Adults with Knee Pain Sought

Clinical Center researchers seek 18-55 year olds with knee pain (patellofemoral or anterior knee pain) for a 2-visit outpatient research study. We are studying how muscle weakness around the knee may lead to changes in knee cap motion and pain. Compensation is provided. Learn how to participate by contacting the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010) or prpl@cc.nih.gov. Refer to study 15-CC-0099. Read more online at https://go.usa.gov/xg34m.

Healthy Volunteers Needed

Partner with NIAID researchers to investigate how antibiotics affect the trillions of good microbes that live on or in our bodies, also known as our microbiome. If you are 21-39 years old and healthy, contact the CC Office of Patient Recruitment, 1-800-411-1222, or prpl@cc.nih.gov. Refer to study 16-1-0078. Read more online at https://go.usa.gov/xng4m.

Study Needs Healthy Children

NICHD seeks healthy children 7 to 11 years old with above average weight to join in a research study. Researchers want to learn if breaking up sitting with short periods of activity improves children’s metabolism and attention. Six outpatient visits on consecutive days of about 3 hours each (Monday- Friday, early evening and Saturday morning) are required. Compensation will be provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://go.usa.gov/xRPAg. Refer to study 17-CH-0130.

VRC Recruits Healthy Volunteers

Vaccine Research Center researchers seek healthy volunteers, 18-50 years old, for a study evaluating an investigational vaccine that targets HIV. Compensation is provided. There is no risk of infection. To learn how to participate, call 1-866-833-5433, email vaccines@nih.gov or visit http://bit.ly/VRC-018.

Volunteers with Diarrhea Needed

The National Institute of Nursing Research invites volunteers of all ages experiencing diarrhea to participate in a research study. Many people suffer from diarrhea every year. In the United States, it leads to about 130,000 hospitalizations and 3,000 deaths a year. Researchers want to test whether a research tool detects pathogens (for example bacteria) that cause diarrhea. The study involves one outpatient visit that may last 2-3 hours and stool sample collection. No compensation will be provided. All study-related tests will be provided at no charge. Parental consent is required for minors. For more information about study 18-NR-0040, call 1-866-444-2214 (TTY 1-866-411-1010) or visit https://go.usa.gov/xP7h5.
Managing Inner-City Pediatric Asthma

BY ADRIENNE BURROUGHS

When managing chronic conditions such as asthma, health care providers need to look beyond the standard doctor’s visits and taking medications as prescribed. Dr. Arlene Butz has devoted her life’s work to investigating the many factors that contribute to childhood asthma. She discussed this work at the first NINR Director’s Lecture of 2019. Her studies of childhood asthma in inner-city Baltimore are prime examples of how complicated it can be to develop home-based interventions for managing chronic conditions.

“I think most of the self-management happens in the home and that’s where we need to help caregivers make the right decisions” about asthma care for their child, noted Butz. One of the critical decisions caregivers make for children with asthma is when to give medication. Butz found through her studies that instead of being given long-term controller medicines, many children are given rescue medication—which is supposed to be used for asthma emergencies—for routine management of their asthma. Butz’s research found that managing medications was only one of many factors contributing to children’s poor asthma control.

During home visits for one of her studies, nurse interventionists reported children having high exposure to secondhand smoke and contamination of nebulizer equipment. This prompted Butz and her team to take a closer look at home environments and whether there were other factors that could be contributing to poor management of the children’s asthma.

A secondary study showed that 37.5 percent of nebulizer tubing and masks from study homes tested positive for environmental allergens such as dog, mouse and cockroach, “This helped us realize the importance of what’s in the home environment,” Butz said.

She also used biomarkers of allergy and indoor exposure (dog, cat, mice, cockroach and second-hand smoke) and found that 83 percent of the children in the study had at least one positive allergen sensitization and 55 percent were exposed to secondhand smoke. By looking at allergens on an individual home level, the study was able to provide personalized interventions—such as mouse traps and trash cans for homes with mouse allergens and mattress covers for homes with dust mite allergens.

Butz’s studies uncovered important lessons that she was committed to sharing with study participants in a meaningful way. She and her team created a short, animated video to communicate study results, instead of a more traditional letter to study participants. The video (https://vimeo.com/261407654) graphically depicts the most important lessons and helps educate the study participants’ families about how to better manage their child’s asthma.

Improved self-management of asthma and other chronic conditions is an ongoing research area. The potential to avoid visits to the emergency room, hospital stays and negative health outcomes is tremendous. If caregivers prioritize the home environment, personalized treatment plans and improved communication efforts, patients’ quality of life can be enhanced and their symptoms better managed.

Butz is professor of pediatrics at Johns Hopkins University School of Medicine with a secondary appointment in the School of Nursing. The full video of her lecture is available at https://video-cast.nih.gov/summary.asp?Live=31581&bhcp=1.

NCCIH Lectures Explore Gut Microbes and Health

This spring, the National Center for Complementary and Integrative Health offers three lectures on the theme of “Gut Microbes: Emerging Insights on Health and Disease.”

On Wednesday, May 9 at 11 a.m. in Lipsett Amphitheater, Bldg. 10, Dr. Maria Gloria Dominguez-Bello will speak on “Gut Microbes in a Disruptive Age.” Mammals are colonized with live microbes—acquired during birth—that play a role in healthy development. Practices such as cesarean section and modern antimicrobial measures can reduce this transmission and disrupt the microbiome. Dominguez-Bello will discuss the effect on risk for immune and metabolic diseases and also how lifestyle changes, such as increasing urbanization, can affect the microbiome. She is Henry Rutgers professor of microbiome and health at Rutgers University and holds a Ph.D. in microbiology from the University of Aberdeen, Scotland.

Dr. Isaac Chiu of Harvard Medical School will lecture on “Bacteria Get on Your Nerves: How Bugs Modulate Pain and Immunity,” on Monday, June 10 at 11 a.m. in Lipsett. He will discuss his research on interactions of the nervous system, the immune system and microbes in health and disease, which may lead to new treatments for inflammation and pain. Knowing more about how bacteria communicate with pain fibers, for example, could tell us more about the mechanisms in pain. Chiu received his Ph.D. in immunology from Harvard Medical School, where he is an assistant professor of immunology. He is a recipient of the NIH Director’s New Innovator Award.

In a rescheduled event, Dr. Sean Brady will present “Watch Your Step: There Is New Chemistry Everywhere,” on Wednesday, June 26 at 9:30 a.m. in Lipsett. He has developed innovative approaches to identify and characterize the huge community of natural products from uncultured bacteria. He will discuss applying these tools to the search for new treatments such as antibiotics and to learning more about how bacteria interact with the surrounding world. Brady is Eynin and Tri-Institutional professor and head of the Laboratory of Genetically Encoded Small Molecules at the Rockefeller University. He received his Ph.D. in organic chemistry from Cornell University.

Natural products, including in relation to the gut microbiome, are a priority area for NCCIH. The lectures will be videocast and are part of the center’s Integrative Medicine Research Lecture Series. To find out more, visit https://nccih.nih.gov/news/events/IMlectures.