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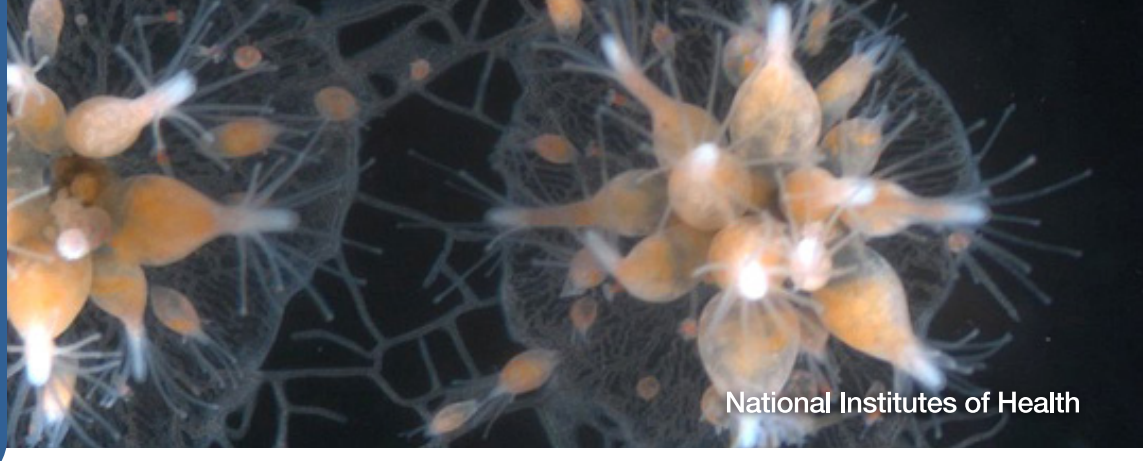


'AN AMAZING STORY'

Rare Disease Patient Finds Renewed Hope at NIH

BY DANA TALESNIK

Living with a rare disease can cause ongoing emotional distress. So much about a rare disease and its progression remains uncertain; treatments and dosing are often experimental. And, it can be tough finding someone knowledgeable enough about the disease to provide reliable, specialized care.

April Murphy, 46, has a rare genetic disorder called methylmalonic acidemia (MMA), a life-threatening metabolic condition that causes severe episodes of illness and long-term complications. Murphy currently is in end-stage renal failure, awaiting a kidney transplant. Despite her condition, she considers herself fortunate.

When April Murphy (l) visited NIH in January, she reconnected with NICHD director Dr. Diana Bianchi.

She visited NIH for the first time in January, when she met NHGRI senior investigator and MMA expert Dr. Charles Venditti, and reconnected with NICHD director Dr. Diana Bianchi, who had counseled and treated her and her mother for an unrelated genetic condition two decades earlier.

"As somebody who works with doctors daily," said Murphy, a surgical assistant in Williamsburg, Va., "what NIH doctors do is not a job to them. It's so much more. They put 110 percent of themselves into what they do to take care of people, and you don't find that everywhere."

First Fetal Patient

Murphy's luck began before she was born. Growing up in the Boston area, she auspiciously came under the care of Dr. Mary Ampola, a biochemical geneticist at

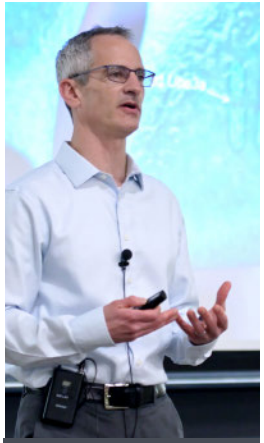
SEE **MURPHY**, PAGE 6

Building entrances look a little different in the age of COVID-19. See a few notable sights, p. 12.

ALSO THIS ISSUE

Treatment Opportunities Seen for Angelman Syndrome

BY CARLA GARNETT



Dr. Ben Philpot

They may have the cheerful faces and demeanor of cherubs, but people with Angelman syndrome (AS), a rare neurodevelopmental disorder, also face significant lifelong challenges, including seizures, problems with balance and movement, and an inability to speak.

"We're interested in developing a treatment for AS first and foremost due to the personal tragedy of the disorder," said longtime grantee Dr.

SEE **ANGELMAN**, PAGE 4

Rare Disease Research Progressing, But Could Go Even Faster

BY ERIC BOCK

NCATS's Dr. Anne Pariser works to accelerate rare disease research.

Getting diagnoses for patients with rare diseases can be a years-long odyssey, said Dr. Anne Pariser at NIH's 10th observance of Rare Disease Day held in the Natcher Bldg. recently.

Rare diseases are conditions affecting fewer than 200,000 people in the United States. The "overwhelming majority" of these diseases are far less prevalent, explained Pariser, director

SEE **RARE DISEASES**, PAGE 8

NBA All-Star Curry Holds Instagram Q&A with Fauci About COVID-19

More than 50,000 people watched Golden State Warriors guard and two-time NBA Most Valuable Player Steph Curry talk with NIAID director Dr. Anthony Fauci about COVID-19 on Instagram Live. The event took place Mar. 26.

During the chat, Curry asked Fauci several questions, including one about what needs to happen before people can attend large gatherings again.

"You need to see the trajectory of the curve start to go down," Fauci told Curry. "We can start thinking about getting back to some degree of normality when the country as a whole has turned that corner and started coming down. Then you can pinpoint cases much more easily than getting overwhelmed by cases, which is what's going on in New York City."

Before the chat, Curry tweeted, "Hyped to talk all things COVID-19 with Dr. Fauci of the @NIAIDNews tomorrow." He encouraged his followers to submit questions using the hashtag #SCASKSFAUCI.

NIAID director Dr. Anthony Fauci used a host of nontraditional media during the month of March to reach as many people as possible about the best way to contain the pandemic. Above he chats with NBA All-Star guard Steph Curry of the Golden State Warriors. The two spoke on Mar. 26, with Curry asking both his own questions and those of his followers on Instagram.

Atrium of Hospital Hosts Concerts

The U.S. Army Band "Downrange" (above) recently performed a repertoire of rock, pop and patriotic music for Clinical Center patients, staff and visitors. Downrange supports armed services personnel as well as Congress, diplomats and special public groups. Below, the University of Maryland Jazz Combo, on a different occasion, played an array of jazz standards. Improvisation is a key component of the group's performances, which feature the music of Duke Ellington, Miles Davis, Sonny Rollins, Wayne Shorter and many others. Faculty members, students and alumni make up the group and enjoy performing America's classical music together.

PHOTOS: DEBBIE ACCAME

Pandemic Preparedness in the Workplace and ADA

During these uncertain times, we must remember to act quickly to effectively accommodate the medical needs of NIH employees and applicants while ensuring those individuals are protected from disability discrimination.

Managers/supervisors should engage in an expedited interactive process with their employees to determine the workplace barriers experienced by the individual and possible immediate accommodation(s) to overcome those barriers (while keeping in mind the general guidelines of ADA disability-inquiries for pandemics). Managers/supervisors should try handling all pandemic-related reasonable accommodation (RA) request approvals through managerial authority if the need is urgent. Still, for any questions or RA denials, they must contact the NIH Reasonable Accommodation Program team (https://www.edi.nih.gov/consulting/reasonable-accommodation/contact), which manages the NIH RA program, immediately.

Learn more about EEOC Guidance regarding Pandemic Preparedness in the Workplace and ADA by visiting https://www.edi.nih.gov/blog/news/pandemic-preparedness-workplace-and-americans-disabilities-act.

NIEHS Cryo-EM Resources Support Fight Against Novel Coronavirus

BY KELLY LENOX

The NIEHS cryo-electron microscopy (cryo-EM) facility, led by Dr. Mario Borgnia, is providing key support to the Duke Human Vaccine Institute (DHVI) in the fight against the SARS-CoV-2 virus, which produces COVID-19. Recently, Borgnia spoke with NIEHS about the research he conducts with Duke's Dr. Priyamvada Acharya.

Cryo-EM is an advanced microscopy platform launched at NIEHS in 2017 as part of the Molecular Microscopy Consortium, along with Duke and the University of North Carolina at Chapel Hill.

"I am so glad we invested in cryo-EM technology," said NIEHS scientific director Dr. Darryl Zeldin. "Mario is doing an outstanding job leading the Molecular Microscopy Consortium, to provide support for the entire region. Our investment is paying off as Mario is working collaboratively with scientists at DHVI to facilitate development of a vaccine against SARS-CoV-2."

Why are you focusing on the so-called spikes of the virus structure?

Borgnia: The spikes that form the so-called corona are viral proteins. Members of the coronavirus family bud out new viral particles from an infected cell by pinching a small bubble of the cell's own membrane.

This envelope surrounds the virus' genetic material, acting as a cloak to prevent detection. The body's immune system does not recognize the virus as foreign, so it does not mount a fight. Yet the virus at this point is still isolated in its own bubble.

Here is where the spike comes into play. If you think of a key and lock, the spike is the key. The lock is a receptor in the human cell. The virus attaches the key in a new cell's lock. It then fuses its envelope with the cell membrane and injects its genetic material into the cell.

But the spikes are also the Achilles heel of the virus, because the immune system can recognize them as foreign material.

During the early stages of viral infection, the body begins generating antibodies against the spikes, or any portion it recognizes as foreign. If it does this faster than the virus replicates in the body, we do not get really sick. The idea of a vaccine is to prime the immune system with the spike protein to increase the concentration of antibodies against it, even before the body detects a live virus.

Once our immune system knows the disease, it has the advantage and can drive the virus away. The goal of our work is to generate a version of the spike that prompts the body to generate effective antibodies.

Dr. Mario Borgnia said that the shape of a protein is closely related to its function, so discovering the shape with tools such as cryo-EM helps scientists gain insight into the job it performs.

PHOTO: STEVE MCCAW

This is very different from HIV, for example, which is much more complicated. HIV mutates in the body so that infected people rarely develop protective immunity, although we are learning tricks to teach the immune system to fight HIV as well.

A major goal in the effort to defeat this [coronavirus] pandemic is finding a way to interfere with the process of cellular infection. A treatment would block the virus's recognition of the target receptor in those who are sick. A vaccine would teach the immune system to make antibodies to neutralize the spikes before disease develops.

Using cryo-EM, we hope to determine the structure of the spike—by itself, in complex with the target receptor, and in complex with neutralizing antibodies.

Where in the process are you right now?

Borgnia: Dr. Acharya's team is working closely with Allen Hsu, here at NIEHS, to optimize cryo-EM grids for SARS-CoV-2 spike samples using the NIEHS Talos Arctica microscope. These are then imaged using the Duke Titan Krios microscope. Dr. Acharya's group is working around the clock together with my team to further optimize the specimens.

Can you explain what optimizing the specimens involves?

Borgnia: To get a structure using cryo-EM, you gather tens of thousands of images of the protein, then average them to obtain a 3-D structure. To do this, the proteins are frozen in a thin layer of ice on a grid, by a process known as vitrification.

By optimizing the vitrification conditions, we can produce cryo-EM grids suitable for high-resolution imaging. We look forward to continuing our work with Dr. Acharya's group to optimize samples of spike variants and complexes for imaging. R

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

IMAGE: ANDY BAXEVANIS, NHGRI

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Angelman

CONTINUED FROM PAGE 1

Ben Philpot at a recent NIH Neuroscience Seminar Series lecture. "We want to help these individuals who are so wonderful yet so challenged in life, and to help their caregivers. We're also motivated because of this incredible opportunity for developing therapeutics."

Kenan distinguished professor at the University of North Carolina, Chapel Hill, and associate director of the UNC Neuroscience Center, Philpot outlined his group's promising potential treatments and clinical biomarkers for the syndrome.

"A hallmark of Ben's research is that he likes to integrate genetic, electrophysiological, neurochemical and behavioral experiments to try to get a more holistic view of these animal models and also their translational potential," said Dr. Andres Buonanno, senior investigator in NICHD's section on molecular neurobiology, who invited Philpot and introduced the lecture.

In 1965, Dr. Harry Angelman, a British pediatrician, first described children showing symptoms of the condition that would later be named for him. Photos of Angelman patients often show them smiling and laughing, Philpot said. They typically demonstrate happy dispositions as well as severe intellectual disability.

"A very defining feature is their lack of speech," he explained. "Individuals often don't speak a single word their entire lifetime, yet they can live a full life."

Approximately 90 percent of people with AS experience frequent seizures, about 80-90 percent have microcephaly (small head circumference leading to poor brain development), 80 percent have rhythmic EEG patterns and about 75 percent have sleep problems.

A single-gene disorder, AS results from deletions or mutations of the gene UBE3A. The syndrome has a high comorbidity with autism and occurs in about 1 in 15,000 individuals.

"Neurotypically, UBE3A is only expressed off the allele we inherit from our mothers," Philpot explained. "The paternal allele is epigenetically silent. In Angelman syndrome, however, the maternal allele has also been silenced due to mutation."

In their studies, Philpot and colleagues use mice genetically modeled with AS. The animals mimic key features of the disorder in humans, such as learning and memory impairments, ataxia and increased susceptibility to seizures.

"There's an incredible burden on this patient population," said Philpot, describing the 60 percent of patients who exhibit multiple seizure types.

Currently, scientists are developing three strategies to treat the disorder—relieve symptoms, reactivate the dormant UBE3A or apply traditional gene therapy.

In efforts to relieve a major symptom—seizures, for example—doctors use anti-epileptic medications, nutritional interventions such as ketogenic or low-glycemic-index diets, and, in rare circumstances, surgery.

The full spectrum of anti-epileptics has varying degrees of efficacy and utility, Philpot said.

"Even with all of these anti-epileptics at our disposal," he noted, "many of these individuals are refractory to the traditional anti-epileptics, so we need yet another line of treatment for seizures in individuals with Angelman syndrome."

One promising new therapeutic for Angelman seizures is cannabidiol (CBD), the non-psychoactive substance Philpot jokingly referred to as a "hippie's disappointment."

Using synthetic CBD, which is about 99 percent pure, Philpot's group has shown reduced seizure duration and severity in AS mice.

"This is the first hint that cannabidiol might lead to some therapeutic benefit for seizures [in humans]," he said, cautioning that safety and efficacy tests need to be performed first in clinical trials before any firm conclusions can be drawn.

"A much more transformative treatment would be to treat the disorder at its genetic core," Philpot said, explaining his group's efforts to reactivate the silent UBE3A gene.

"We were able to show that a drug, Topotecan, can very powerfully turn on the paternal allele of UBE3A," he said. "This is really exciting because it's an FDA-approved compound, so it was already cleared for safety and use."

The drug worked both *in vivo* and *in vitro* in mice for up to a year after injection.

Still, Philpot said, researchers' excitement has been tempered by several serious limitations: Topotecan comes with some toxicity, including the neutropenia commonly associated with chemotherapy. They also do not yet know how long the compound remains effective in the cortex.

Researchers have identified other small molecule compounds that they can deliver

One new promising therapeutic for Angelman seizures is cannabidiol (CBD), the non-psychoactive substance Philpot jokingly referred to as a "hippie's disappointment."

PHOTOS: MARLEEN VAN DEN NESTE

"We're really just beginning to scratch the surface about what types of information we can get from the EEG biomarkers," Philpot said.

peripherally—and less invasively—but with similar gene-reactivating effects on AS mice. Further study is necessary.

Philpot also emphasized the need to develop acceptable measurements—biomarkers—for use in human clinical trials.

"People have had ideas of what to use for therapies before they're actually ready to go to the clinic, before there were good outcome measurements," he pointed out.

Philpot suggested several features he'd want in an ideal AS biomarker: clinically relevant, objectively quantifiable, minimally invasive, highly penetrant and reversible in the mouse model.

To evaluate one potential measuring tool, he and colleagues began analyzing enormous amounts of EEG data from AS patients and comparing the data with results from mice models. The scientists looked at delta waves and sleep spindles, or bursts of neural activity in the central nervous system .

"We're really just beginning to scratch the surface about what types of information we can get from the EEG biomarkers," Philpot said.

He ended his slide set with an animation he called "the 'I Have a Dream' portion of the talk," showing an illustration of unhealthy mutated UBE3A genes, depicted as gray.

"The dream is we're going to treat [AS] with a small molecule or some other type of therapy that could come in like a flurry of snowflakes and reactivate this dormant allele and make the neurons happy and healthy and pink and try to help these individuals with Angelman syndrome," he concluded. "That's really what our ultimate goal is."

NIH funders of Philpot's research include NICHD, NIMH and NINDS. R

SOUND HEALTH

Science and Music: A Meeting of the Minds

Can science tell us why we create music and how the art form might improve our health? Those questions—and live jazz improvisation—entertained a packed crowd at Music and Science. The recent lunchtime event was hosted by NIEHS and the Research Triangle Foundation.

Headlining the event were bassist John Brown, director of Duke University's jazz program and professor of the practice of music, and Dr. Richard Mooney, professor of neurobiology at Duke. His lab studies the neurobiology of hearing and communication, with special emphasis on the neural mechanisms of vocal learning, production and perception.

Brown and guitar accompanist Kevin Van Sant opened with a jazz set. The discussion that followed touched on music's mysteries and appeal, complemented by hard science.

"I love talking about what we're doing, especially with this audience. People seem to care," said John Brown (r), with accompanist Kevin Van Sant.

Mooney, a classically trained guitarist, described the brain and ear connection as a closed loop—known as a recurrent network. The cochlea does more than just deliver sound. The brain, cochlea and internal chemistry work together to influence how we hear, from assisting active listening to amplifying sound. Musicality in speech is essential to communication.

"There are people who have lesions in the right frontal cortex who lose a kind of musicality, making their speech very hard to understand," said Mooney. "Without emotional inflection and content, speech becomes almost incomprehensible." He pointed out other ways music and the brain interact:

• Although Alzheimer's patients struggle to remember, they can sing along effortlessly with songs from their childhoods.

• Cochlear implants have made it possible for the deaf to hear again, but because technological limitations result in low music spectrum sensitivity, which is necessary for appreciating music, they typically do not like to listen to music.

• Stutterers can sing fluently.

"There's a lot of debate over whether there is some kind of innate predisposition to music," said Mooney. "My guess is that it's our way of exploring something our minds can't get to any other way. Most people make music, whether they know it or not."

Discussing improvisation, Brown and Van Sant both described it as an intuitive process that requires musicians to listen intently and be sensitive to minor changes in tempo and mood. "People often say there's a connection between music and science that we don't really understand," said Brown. "Well, this is as tangible as it gets, breaking down how our brains respond to music, trying to put a finger on this connection."

The lunch was part of the Sound Health Initiative, a partnership between NIH and the Kennedy Center that started in 2017. NIH has awarded $20 million over 5 years to support the initiative's first research projects.—**John Yewell**

"The reality is we don't know the science behind how music influences health, so we're trying to start having those conversations," said Dr. Laura Thomas (r), shown with Dr. Brandy Beverly.

PHOTOS: STEVE MCCAW

At left, Bianchi first met Murphy in 1999 at an event at Tufts celebrating the publication of the textbook *Fetology: Diagnosis and Management of the Fetal Patient*, which Bianchi co-authored. Seated in front, Murphy is surrounded by (from l) Bianchi, Dr. Mary Ampola and April's mother, Theresa Murphy. At right, Murphy is shown with her daughter Victoria, granddaughter Olivia and her mother Theresa.

Murphy

CONTINUED FROM PAGE 1

Tufts-New England Medical Center, who first treated Murphy in her mother's womb.

Incredibly, just a few years before Murphy was born, a researcher determined that some patients with MMA responded to large amounts of vitamin B12 (cobalamin). That discovery inspired Ampola to try a revolutionary treatment after amniocentesis confirmed that Murphy had inherited the vitamin-responsive type of MMA.

In 1973, with support from NIH and March of Dimes grants, Murphy's mother received oral, then intramuscular injections of cobalamin for the last 2 months of pregnancy; the vitamin entered the placenta to treat baby April. The groundbreaking case was reported in 1975 in the *New England Journal of Medicine*.

"From my perspective," said Bianchi, who first met Murphy in 1999 through Ampola, then her colleague at Tufts, "as someone interested in prenatal testing and field treatment, April is really a very special and legendary person because she was the first person ever to be treated *in utero* for a genetic disorder."

At that time, MMA patients didn't get diagnosed until symptoms appeared in infancy or later in childhood. In Murphy's case, a family tragedy saved her life. Her older sister died at age 3 months. Posthumous testing revealed that her sibling had MMA. While the condition is now routinely tested as part of newborn screening, it's still unusual to make a prenatal diagnosis.

"The cobalamin-A form of the disorder, what April has, within the spectrum of MMA is considered milder," said Venditti, "but it's still extremely dangerous...With this type, there's a partial response to B12, but if a patient doesn't get enough vitamin, he or she can go into a coma or have other serious complications."

★ ★ ★

"It really makes the biggest difference in my life. You guys truly are the superheroes of medicine."

~APRIL MURPHY

★ ★ ★

Lucky in Life

Growing up, Murphy had a normal childhood. She logged her diet daily, knew her limitations and took full responsibility for managing her condition, all under the supportive watch of Ampola. Murphy did have some scares, and was hospitalized a few times for metabolic acidosis, but quickly recovered.

April with her mother, Theresa

She has taken hydroxocobalamin most of her life. Terrified of needles, she'd squirt the liquid vitamin into ginger ale. Drinking the elixir daily maintained her methylmalonic acid levels.

Murphy poses with the NHGRI clinical team: (from l) Dr. Ryan Peretz, senior investigator Dr. Charles Venditti, Murphy, Dr. Irini Manoli, nurses Carol Van Ryzin and Susan Ferry, and Dr. Jennifer Sloan.

After high school, Murphy gave birth to a healthy daughter, and now has two grandchildren. Her daughter, as well as her two younger sisters, are MMA carriers but none of them have the recessive disorder.

As an adult looking back, Murphy is grateful for the meticulous care she received, and the experimental prenatal treatment that contributed to her better outcome at birth and beyond.

"Doctors have told me, after all my testing, that there could have been neurocognitive damage, possibly physical issues," said Murphy, "so it really made a difference that they [gave my mother the B12] *in utero* versus waiting until I was born."

A Genetic Scare

Twenty years ago, Murphy and her mother met with Bianchi, who was launching a genetic research project at Tufts-New England Medical Center on cancer in families. Murphy's mother had survived breast and ovarian cancer and today remains cancer-free. Bianchi would counsel and treat them after they both tested positive for the BRCA gene.

"I come from a long line of strong women," said Murphy, undeterred by the diagnosis. "It was great to find out so early on so that I could make decisions for my future before anything happened."

Ten years ago, a preventative oophorectomy sent Murphy into early menopause. The accompanying extreme fatigue lasted an unusually long time. It turned out, the fatigue was caused by dangerously high acid levels, which would take years to stabilize. A nephrologist later diagnosed her with end-stage renal failure.

Toward New MMA Treatments

NHGRI's Venditti has devoted much of his career to studying MMA. He began seeing patients in 1999 while a genetics fellow at Children's Hospital of Philadelphia. Doctors tried to discourage him from working on MMA, arguing that it wasn't treatable, but, encouraged by many parents, he was determined to find better therapies.

"Now we have a lot more options for the patients and I really think it won't be long until we have gene therapy," said Venditti. "We're going to get this to work."

He and his colleagues at NHGRI have teamed up with several biotech companies and are developing promising new genomic therapies for MMA. He also oversees an MMA natural history study in the Clinical Center that has enrolled more than 200 patients; Murphy is the newest member of the cohort.

"One needs to understand the natural history of MMA before a new treatment is tested," said Venditti, "and answer the questions of what the effects will be downstream on the patient." The NHGRI natural history study helps track metabolic parameters, nutrition patterns, bone phenotypes, symptoms over time, genetic effects and, in concert with lab work, has identified new biomarkers for treatment.

"I counseled April more than 20 years ago," said Bianchi, "but to see her again, it's such a privilege because you get that long-term perspective. It's an amazing story because it's a rare but treatable genetic disorder, and there have been a lot of advances that really translate to patient care."

Venditti is leading a natural history study on MMA, of which Murphy is the newest member.

Looking Ahead

During Murphy's recent NIH visit, Venditti and his NHGRI team members Dr. Irini Manoli and Dr. Jennifer Sloan reassured her that renal failure was a consequence of MMA and that there was nothing she could have done to stop the progression. She also came away comforted that NIH doctors and resources are just a few hours from home.

Murphy is scheduled for a kidney transplant this spring. Neither sister was a match, so she and her wife are participating in a kidney swap program. Murphy is otherwise deemed in good health and optimistic about the future.

"In Massachusetts, I grew up my whole life having Dr. Ampola as my hero, always there to take care of me," said Murphy. "When I moved to Virginia, there was an emotional loss. It was hard to find anyone to take care of me here who knew anything about MMA."

She worried about where she'd turn if her condition changed or if she had any sort of emergency. "Daily life here, medically, has been a scary thing. But...now I have Dr. Bianchi and Drs. Venditti and Manoli and the MMA team in Bethesda. If anything should go wrong, I have people I can count on to take care of me."

In tears, Murphy added, "It really makes the biggest difference in my life. You guys truly are the superheroes of medicine."

Organizations displayed posters and exhibits during Rare Disease Day at NIH. Several exhibits highlighted NIH-supported rare diseases research. At right, panelists discuss non-traditional approaches to improving access for rare diseases.

Rare Diseases

CONTINUED FROM PAGE 1

of the Office of Rare Diseases Research at NCATS. In total, there are 25 million-30 million people with rare diseases in the United States.

The daylong event included scientific talks, patient stories, poster sessions, panel discussions, art exhibits and more.

About 85 percent of these diseases are single-gene disorders. Only 5 percent of rare diseases have an FDA-approved therapy. At the current rate, it's going to take thousands of years to get treatments for all rare diseases.

To speed up drug development, Pariser said, "We're currently trying to transition from a one-disease-at-a-time model to a many-diseases-at-a-time model."

Over the past 10 years, what's happened scientifically in rare diseases research has been "breathtaking," said NIH director Dr. Francis Collins, in videotaped remarks. While doctors can do a better job diagnosing and treating these conditions, he noted, there have been several advances in therapies for rare diseases in recent years.

This past October, the FDA approved a treatment for cystic fibrosis, a life-threatening genetic disorder that causes serious damage to the lungs. Until recently, there was only treatment for symptoms, Collins explained. Thanks to decades of work, 90 percent of patients with cystic fibrosis are seeing "remarkable" responses. Collins helped lead pioneering studies of the disease.

"That is incredibly inspiring to see, and we want to replicate that many times over," he said.

The FDA has approved two therapies for spinal muscular atrophy, a group of hereditary diseases that progressively destroy motor neurons. The agency will soon review another potential treatment, continued Collins.

Additionally, he said, evidence from clinical studies suggests that gene therapy can be used to treat, and possibly cure, sickle cell disease. One version of gene therapy replaces a disease-causing gene with a healthy copy of the gene.

Researchers are also studying how to safely use gene-editing technologies, such as CRISPR-Cas9, to turn on fetal hemoglobin in sickle cell disease and also to fix genetic mutations that cause other rare diseases.

"The landscape's really changing and changing for the better. I know it's not changing as fast as many of you would like to

Rare Disease Day at NIH was held in Natcher Conference Center for the second year in a row. At right, Dr. Chip Chambers (l), assistant clinical professor of surgery, Vanderbilt University Medical Center, founder and president of the DADA2 Foundation, and Dr. Amanda Ombrello, associate research physician, adult and pediatric rheumatologist at NHGRI, share their rare disease stories.

PHOTOS: JONATHAN FROST, MEGAN SCHARTNER

Clinical Center CEO Dr. James Gilman said 57 percent of all CC patients have a rare disease.

see," Collins concluded. "I want to assure you we are aware of that and doing everything we can with the resources that Congress—as representatives of all taxpayers—has given us."

Patients with rare diseases need to be part of the FDA's medical product review process, said Sen. Amy Klobuchar (D-MN) in videotaped remarks. She spoke on behalf of the bipartisan and bicameral Rare Disease Congressional Caucus.

Three years ago, passage of the 21st Century Cures Act was an important milestone for incorporating patient experiences into the drug approval process, she noted. Klobuchar said more work must be done to ensure that the FDA considers patient experiences and patient-focused drug information as part of the risk-benefit assessment.

This patient-centered approach was visible throughout the day. In one panel discussion, researchers and patient advocates discussed ways to shorten the often long, frustrating time patients can wait for a rare disease diagnosis. In another session, panelists addressed the potential advantages of and accompanying challenges in developing individualized therapies for rare disease patients. A third panel examined non-traditional ways for patients and clinicians to tap into rare disease resources and information.

Congress included language in the FY 2020 budget directing the Government Accountability Office to conduct a study of the impact rare diseases have on the economy. The research is an important step in learning how much rare diseases affect patients and families, said NCATS director Dr. Christopher Austin. The results of the study will be published in 2022.

"You all [patients, their families and patient advocates] made this possible," said Austin. "You worked with NIH and investigators to try to bring together all the things that it takes in order to make this research possible. I want to thank you for that and ask you to continue with that energy, determination, willingness to be creative and take risks. We're with you on that."

Rare Disease Day at NIH is sponsored by NCATS and the Clinical Center.

NCATS director Dr. Christopher Austin welcomes attendees to Rare Disease Day.

UPCOMING EVENTS

Riegel To Present NINR Director's Lecture

On Wednesday, Apr. 29, Dr. Barbara Riegel will virtually present the second 2020 NINR Director's Lecture from 1 to 2 p.m. via https://videocast.nih.gov/. In her presentation, "At the Intersection of Self-Management and Symptom Science," she will discuss her research in self-care, which includes treatment adherence, condition monitoring and self-management of symptoms.

Dr. Barbara Riegel

Riegel is a professor of gerontology at the University of Pennsylvania School of Nursing and co-director of the International Center for Self-Care Research. She began studying self-care early in her career while a clinical researcher in an acute care setting when hospitals were just beginning to recognize that heart failure was a primary reason for hospital readmissions. Riegel has developed theory and self-report measures of self-care that are used worldwide.

She has received numerous honors and awards including the Distinguished Scientist Award from the American Heart Association, Sigma Theta Tau International Nurse Researcher Hall of Fame and the Barbara J. Lowery Award from the Doctoral Student Organization at the University of Pennsylvania.

The event is free and open to the public. For more information and to register, visit http://ow.ly/jGTX50yWJEc.

Postbac Poster Day 2020 Is Going Virtual

NIH has been forced to cancel the face-to-face 2020 Postbac Poster Day due to the coronavirus outbreak. However, virtual Poster Day has been scheduled for the end of April. More than 875 postbacs have registered to present. The virus outbreak has led to the cancellation of many important events for the NIH community. We invite you to help us make sure this event, rather than being cancelled, is the best Postbac Poster Day ever.

Postbac Distinguished Mentor Awards will be announced on the OITE website on Apr.30.

Poster Day provides an opportunity for postbacs to share the research they have been conducting at NIH and develop their scientific communication and networking skills. Posters will be reviewed by teams of graduate students, postdocs and staff scientists/clinicians. The authors of the top 20 percent will receive a letter acknowledging their accomplishments. Investigators, staff scientists, other trainees and scientific administrators can make an important contribution to poster day by assisting the postbacs with poster preparation and participating in the virtual event (watch for email instructions). For more information, visit https://www.training.nih.gov/virtual_postbac_poster_day.

Dr. Lisbeth Nielsen is director of NIA's Division of Behavioral and Social Research.

Nielsen To Lead NIA Division

Dr. Lisbeth Nielsen has been named director of the National Institute on Aging's Division of Behavioral and Social Research (BSR). She has a long history of leadership in the behavioral and social sciences at NIH. She served for 15 years as a program director and chief of BSR's Individual Behavioral Processes Branch. She also held leadership roles in the NIH Science of Behavior Change Common Fund program and the trans-NIH basic behavioral and social sciences opportunity network.

Prior to joining NIH, Nielsen conducted research in the affective and decision science of aging at Stanford University.

Throughout her research career, Nielsen has built bridges linking psychological and behavioral science to economics, genetics, neuroscience, biology, epidemiology, social science and biomedicine, at all levels from basic to translational research. She was instrumental in launching new areas of research in subjective well-being and the social, affective and economic neurosciences of aging.

Nielsen helped initiate several innovative research networks linking behavioral and population scientists to tackle questions related to the influences of stress on physical health and on the potential for midlife reversibility of health risks associated with early-life adversity. She is an advocate for the study of aging processes across the full life course, including research on early-life influences on later-life outcomes and on processes in midlife that play a causal role in shaping trajectories of aging.

"Dr. Nielsen's efforts have enhanced the impact of aging-related research and created meaningful opportunities for behavioral and social scientists to participate in high-level and significant NIH scientific initiatives," said NIA director Dr. Richard Hodes. "Her impressive and accomplished background and experiences make her exceptionally qualified to lead this important division at a time of great scientific opportunity."

"NIA's Division of Behavioral and Social Research is among the most influential and exciting behavioral and social science funding organizations in the U.S., and I look forward to leading our talented and creative staff," Nielsen said.

"Our work will continue to evolve to encompass a wide range of behavioral and social science approaches to understanding Alzheimer's disease and related dementias; embracing life course research on the developmental origins of aging processes; extending our focus on midlife prevention of the chronic diseases of aging; and promoting a range of rigorous mechanistic approaches to understanding and advancing behavior change at the individual and organizational levels."

Nielsen also highlighted the division's role in integrating life-span developmental and social science approaches into the broader geroscience agenda, to understand how behavior and the social environment impact the lifespan, health span and the development of age-related diseases, including Alzheimer's disease.

"Multiple approaches—from molecular to social—are needed to understand individual and group differences in the pace of aging and to tackle the growing and disturbingly large health disparities in the United States, a topic that has always been at the forefront of BSR efforts," said Nielsen.

She earned her Ph.D. in cognitive psychology and cognitive science from the University of Arizona, a master's degree in psychology from Copenhagen University and a B.A. in philosophy from Rhodes College. She is a fellow of the Academy of Behavioral Medicine Research, the Association for Psychological Science and the Mind and Life Institute.

LAST LAP LOGGED

Moore Retires After 43-Year Career

BY ERIC BOCK

Jerry Moore recently retired after a 43-year career at NIH. He served as the NIH regulations officer in the Office of Management Assessment's Division of Management Support. In this role, Moore oversaw and managed agency regulatory activities.

"Jerry has provided our teams with expert guidance, stewardship and an unwavering commitment to deliver management excellence on regulatory matters, requirements and processes to assure regulatory compliance," said his director, Anna Amar. "Our team in OMA will miss Jerry's leadership and hands-on, in-the-trenches management style and work ethic, and we're certain our colleagues and stakeholders across the Department of Health and Human Services and NIH will miss him all the same."

Moore received his bachelor's and master's degrees from the University of Maryland. He first learned about NIH when he worked for the University of Maryland's then Office of Resident Life. At the time, he was organizing a career-development program for students in his residence halls. He stumbled across an NIH vacancy announcement for a management analyst position and applied.

"It was really unexpected. I had just taken on a new role with Resident Life and had not anticipated going to NIH," he said. "Like a lot of people, I thought, 'I'll be at NIH for a couple of years and see how it works out.' It's funny to me thinking about that 43 years later."

At NIH, one of the first projects he completed was a pilot study to evaluate flexible workplace schedules. The study analyzed the feasibility of allowing employees to modify their work schedules based on what was most convenient for them.

"We've come a long way since that initial cautious test of flexible working hours," said Moore. "At that time, the concept of allowing your employees to choose what their work schedules looked like was revolutionary."

In his most recent role, he helped to maintain NIH regulations for the HHS secretary. Most of NIH's regulations pertain to grant programs, peer review, standards of

An avid runner who was a longtime leader and member of NIH Health's Angels Running Club, Jerry Moore recently retired after 43 years at NIH.

care for retired chimpanzees, loan repayment programs, conflict of interest and the conduct of persons and traffic on NIH's campus. When Congress enacted new legislation that impacted NIH, Moore worked with appropriate program management and staff to ensure that necessary regulations were in place to implement the legislation .

Additionally, his office managed the NIH review of many draft regulations and guidance documents written by HHS agencies and other departments. He said,"NIH has a wealth of biomedical research-based knowledge and expertise that enables NIH reviewing offices to provide valuable advice to the other agencies and departments concerning their respective draft regulations and guidance documents."

Moore, an avid runner for 33 years, was a longtime leader and member of the NIH Health's Angels Running Club. Many of the people he met through the club and ran with are now scattered across the world. His active role in the club and the relationships that he developed with people across NIH enhanced his knowledge and understanding of the intramural, extramural and administrative communities and the roles they all play in helping NIH achieve its mission.

Moore enjoys coming back to campus to help with the annual NIH Institute Relay, an event that he and his teams won several times. The race brings reliable fun and good cheer to the institutes and centers. People who don't normally mix come together to run in five-person teams.

"Runners of all skills and abilities come to the event without egos or concerns about their position or status at NIH. They are just out there having fun," he said. "I'm proud of the role that I played in helping to make the Institute Relay a lasting tradition for the NIH community to enjoy each year."

In retirement, Moore hopes eventually to go back to school to complete the coursework needed to finish a doctoral program in public administration he started earlier in his career and do some writing.

Recently, he accepted a part-time contract position to help support the NIH Regulations Program. "You really get attached to NIH and committed to its mission and supporting researchers and everything they do. It's a unique agency," he said. "It doesn't take long for somebody new to NIH to realize this is a really special place."

Healthy Volunteers Needed

NIDDK researchers seek healthy volunteers (18-45 years old) to participate in a study investigating how dopamine affects body weight and eating behavior. Participants must be able to visit the Clinical Center for 5 consecutive days to pick up food and then have a 5-day inpatient stay. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010) or email prpl@cc.nih.gov. Read more at https://go.usa.gov/xPTBn. Refer to study 18-DK-0132.

Adults Needed for Study of Gum Disease

NIDCR seeks adults with and without gum disease (periodontal disease) to join a research study. Researchers want to learn how a person's immune system affects the health of the mouth. You will have two outpatient visits; oral exam; dental X-rays and photos; blood, urine and saliva collection; and gum biopsy. Study-related tests and procedures are provided at no cost. Compensation will be provided. For more information, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 12-D-0100. Read more at https://go.usa.gov/xpuTQ.

Healthy Volunteers Needed

Healthy volunteers are needed for a research study on traumatic brain injury at the Clinical Center. Compensation is provided. To learn how to participate, call the Office of Patient Recruitment at 866-444-2214 (TTY 800-877-8339) or email prpl@cc.nih.gov. Refer to study 15-CC-0164. Read more at https://go.usa.gov/xpPQV.

Patients with Liver Cancer Needed

Did you know that primary liver cancer is the second most common cause of cancer-related deaths worldwide? Researchers at the National Cancer Institute want to better understand liver cancer to help design better treatments. Contact the Clinical Center Office of Patient Recruitment at 866-444-2214 (TTY 800-877-8339) or prpl@cc.nih.gov. Refer to study 20-C-0006. Read more at https://go.usa.gov/xpJ2D.

Patients with SAA Needed

NHLBI researchers are studying a new therapy for patients diagnosed with severe aplastic anemia (SAA). Researchers are evaluating if sirolimus can help prevent the relapse of SAA once cyclosporine treatment has stopped. All study-related medications, tests or procedures are at no cost to you. For more information call the Office of Patient Recruitment, 1-800-411-1222 (TTY 1-800-877-8339). Read more at https://go.usa.gov/xnuz3. Refer to study 17-H-0019.

Youngsters with Diabetes Sought

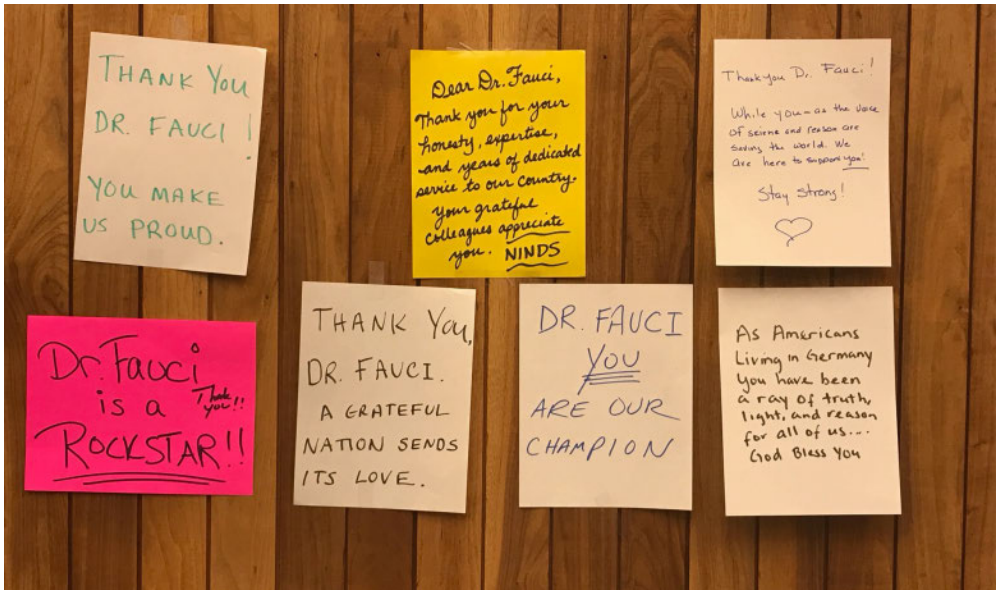
Metformin-related gastrointestinal side effects (bloating, diarrhea, cramping, nausea and vomiting) are common barriers to treatment in youths with type 2 diabetes (T2D), in whom there are no other oral FDA-approved alternatives. NIDDK researchers need your help to test if taking a daily fiber supplement could improve tolerance of metformin. Compensation is provided. If you know a 10- to 25-year-old diagnosed with T2D and needing metformin treatment, call the Office of Patient Recruitment, 866-444-2214 (TTY 800-877-8339) or email prpl@cc.nih.gov. Refer to study 20-DK-0018. Read more at https://go.usa.gov/xdJ6k.

Signs of the Times Emerge on Campus in Pandemic Era

Not Business as Usual. Above and right, Commissioned Corps members screen people with temperature checks at the Clinical Center's south entry. Signage advises patients, staff and visitors about new CC safety policies due to COVID-19 precautions.

PHOTOS (EXCEPT WHERE NOTED): CHIA-CHI CHARLIE CHANG

At left, employees use a newly designated staff-only entrance to the Clinical Center. At center, Occupational Medical Service personnel staff a call center in Bldg. 10. At right, while some building entrances are closed, the NIH Blood Bank remains open and in need of donations.



In a Bldg. 31 elevator lobby, handwritten notes are posted to NIAID director Dr. Anthony Fauci, who has become the nation's expert on all things COVID-19.

PHOTOS: KATHLEEN EASTBERG