



## ‘NO OTHER PLACE IN THE WORLD’ Three Young Siblings Participate in First-in-Human Gene Therapy Trial

BY DANA TALESNIK

Five years ago, a family in Sweden finally got a diagnosis for their 3-year-old son who was struggling with speech and balance. After 18 months of testing, the medical team pinpointed the culprit. It wasn't good news.

The little boy has an ultra-rare, fatal disease, as do his identical twin sisters. There was nowhere to turn, or so they thought. Then they found NIH, igniting a spark of hope.

Hampus Flysjo, who turns 8 this month, and his 6-year-old sisters, Isabella and Julia,

have a neurodegenerative disease called GM1 gangliosidosis for which there is no treatment. This progressive disease destroys neurons in the brain and spinal cord, causing profound atrophy and loss of motor skills. There's a continuum of severity. Children with their subtype typically live only until their early teens.



Niclas Flysjo with son Hampus, at the Clinical Center

“It was emotional when we got the diagnosis,” said their father, Niclas, from a room in the pediatric wing in the Clinical Center in April. “We [initially] were told there were no treatments and no research into this disease.”

Meanwhile, Dr. Cynthia Tift, deputy clinical director of the National Human Genome Research Institute, had been studying this disease for more than a decade, following dozens of patients with GM1 or the related GM2—also known as Tay-Sachs disease—as part of a natural history study.

### An enzyme deficiency

GM1 gangliosidosis is caused by a faulty copy of the GLB1 gene, which when healthy instructs the body to produce an enzyme called beta-galactosidase. This enzyme breaks down and recycles fat-sugar molecules called gangliosides found in neurons that are responsible for brain signaling.

SEE FLYSJO, PAGE 6



Dr. Ziyad Al-Aly

## URGENT RESPONSE REQUIRED Costs of Long Covid Becoming Clear

BY ERIC BOCK

The toll of Covid-19 hospitalizations and deaths is just the tip of the iceberg, warned Dr. Ziyad Al-Aly during a Covid-19 scientific interest group lecture. The consequences of the infectious disease's long-term effects lie just below the surface.

“We need to focus on the long haul and what's beneath that tip,” said Al-Aly, chief

SEE LONG COVID, PAGE 10

## NIH TO NFL Former Intern Graduates to Pro Gridiron Career

BY CARLA GARNETT

NIH is accustomed to its trainees rising to super success after leaving, but Zion Johnson took it to a whole new level recently. The Los Angeles Chargers selected the former NIH Pathways intern and First Team All-American offensive lineman as their first round pick (number 17 overall) in the 2022

SEE NFL, PAGE 4



Former NIH Pathways intern Zion Johnson accepts formal appointment to new job.



Fellows create plush life for kids. See p. 12.

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**New Daily Digest of Events Debuts**

The NIH Calendar of Events and Daily Digest email is now the primary method for notifying staff of events aimed at a subset of NIH staff.

Each morning, staff will receive the digest. It will include previously submitted and newly added events occurring that day, registration reminders, links for more information and the capability to save events to your Outlook calendar.

The NIH-Staff email list no longer accepts most events for distribution. Activities with broad interest such as town halls or Take-Your-Child-to-Work Day and non-event related messages that are pertinent to the entire NIH community will continue to be shared via the all-staff email list.

For details, visit: <https://employees.nih.gov/pages/all-staff-transition.aspx>. Questions? Reach out to [odocplnquiries@od.nih.gov](mailto:odocplnquiries@od.nih.gov).

**Mosquito Day Webinar Set, Aug. 16**

How will climate change affect mosquito-borne diseases such as malaria, dengue fever, yellow fever, chikungunya and Zika? Two experts will weigh in during NIAID’s Mosquito Day webinar on Tuesday, Aug. 16 from 11 a.m. to 12:30 p.m. ET.

Dr. Matthew Thomas, professor at the University of Florida, will discuss current knowledge and priorities for future research to improve understanding of mosquito-parasite-temperature interactions and better predict responses to environmental change. Dr. Elizabeth McGraw, professor at Penn State University, will discuss the current literature and recent work in her lab, in this evolving field.



*Aedes aegypti* mosquitos can transmit the Zika virus.

PHOTO: NIAID

To register, visit [https://nih.zoomgov.com/webinar/register/WN\\_TBR9Rb2TRyq3zxva-NHgCQ](https://nih.zoomgov.com/webinar/register/WN_TBR9Rb2TRyq3zxva-NHgCQ). For sign language interpretation or other reasonable accommodation, email [venera.barsaku@nih.gov](mailto:venera.barsaku@nih.gov) in advance.

**New Express Shuttle Route Debuts**

A new express shuttle service now runs between the Medical Center Metro (inside loop) and the south lobby of Bldg. 10.

The shuttle operates on weekdays from 7 a.m. to 7 p.m. to provide transportation to and from the Clinical Center. For a schedule of shuttle routes, visit <https://go.usa.gov/xJM9w>.

If you have any questions, contact the ORS Division of Amenities and Transportation Services at (301) 402-8981.



Santa Claus and his motorcycle elves from the Montgomery County Police Department and the NIH Police meet at the Children’s Inn for an annual Christmas in July celebration.

PHOTOS: SHANNON GRAVERAN/CHILDREN’S INN

**90+ DEGREE HEAT NOTWITHSTANDING  
Inn Celebrates ‘Christmas in July’**

On July 22, Santa Claus and his motorcycle elves from the Montgomery County Police Department and the NIH Police made their way to the Children’s Inn at NIH to take part in the annual Christmas in July celebration.

Despite soaring temperatures, Santa dressed in his customary faux-fur-trimmed outfit and was greeted by snow (albeit manufactured via machine), Christmas carols on the loudspeaker and a cluster of elves ready to greet him and help hand out gifts.

After visiting with the crowd and wishing everyone a Merry Christmas in July, Santa sat in a rocking chair on the playground and began calling families up to receive personalized gift bags donated by inn supporters.



At left, Santa sits in a rocking chair on the playground and calls up folks for gift bags donated by inn supporters. At right, a youngster waves from Santa’s “motorsleigh.”

## MIX OF CHALLENGES, JOYS

### Researchers with Disabilities Discuss Work Experiences

BY EDDIE YAGO

From “living with disabilities” to “thriving with disabilities,” this was Dr. Bonnielin Swenor’s motto when she founded the Johns Hopkins University Disability Health Research Center. However, sparking a paradigm shift in people’s perspective of disability doesn’t come easy. It starts with sharing experiences.

“Disability is not something to overcome. It is a part of my identity,” said Swenor, who alongside Drs. John Dennehy and William Jacobs, discussed the joys and challenges of disability during a June 28 NIAID diversity and inclusion panel.

NIH’s Dr. David Kosub moderated the discussion and shared his own insights as a scientist with retinitis pigmentosa.

Currently a health science policy analyst in the Office of the Director, Kosub described the challenges of working on the lab bench with a condition that causes progressive vision loss, recalling a seminal moment early in his career.

He was performing a mock HIV experiment with his mentor standing over his shoulder. His principal investigator stated, after overseeing the trial run, that Kosub would not be allowed to work with infected blood out of concern that he might accidentally be exposed to the virus.

Experiences like these aren’t unique to Kosub. Swenor described feeling that her career ended before it began when she experienced a retinal hemorrhage. After a period of depression, she realized that she was internalizing the societal stigma towards individuals with disabilities.

Swenor noted that medical models of disability promote negative stereotypes and ignore how people with disabilities view themselves, despite more than 67 million Americans having a disability.

Swenor concluded that the best way to shift the paradigm to “thriving with disabilities” is to be anti-ableist by continuously including people with disabilities and by increasing accessibility.

Dennehy, a professor of biology at Queens College of the City University of New York, has been deaf in both ears since he was 2½ years old. He described his early experiences as having been

“mainstreamed” to public schools, where the needs of people with disabilities were not necessarily being met. He learned to hide his deafness due to discrimination, bullying and lowered expectations of superiors.

Dennehy learned to rely heavily on lip-reading, which has become nearly impossible due to mask-wearing during the Covid-19 pandemic.

He shared a list of Do’s and Don’ts when speaking with someone who is deaf.

**Do:** Get someone’s attention with a tap. Rephrase a statement with different words.

**Don’t:** Repeat the same words louder. Get frustrated and dismiss an ongoing conversation as it can be very demoralizing.

Jacobs, a professor of microbiology and immunology and molecular genetics at the Albert Einstein College of Medicine, was diagnosed with retinitis pigmentosa at age 6. The condition has significantly reduced his field of vision from 110 degrees to 10 degrees, which he compared to looking through a straw.

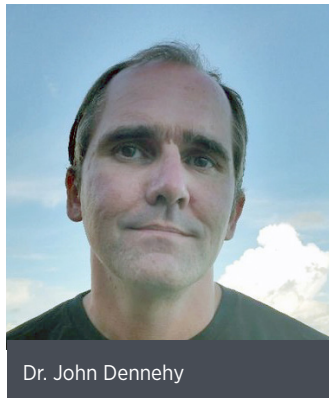
“Reading,” Jacobs explained, “is very time inefficient.”

While hopeful for a remedy in gene therapy, he remains optimistic. A chance meeting with the blind Judge Zak Yacoob, an anti-apartheid activist and a former justice of the Constitutional Court of South Africa, changed Jacob’s perspective on life.

“You have a disability, you are not disabled,” Yacoob told him. The judge had overheard Jacobs complaining about his condition.

Earlier that day, Jacobs had fallen down a flight of stairs due to poor lighting. Recalling this during the conversation, he emphasized the importance of providing accommodation to persons who are visually impaired or blind, such as having appropriate lighting, spaces that are safe and accessible and working with someone who can assist with regular day-to-day professional activities when needed.

Yacoob’s words ring true for many individuals with disabilities. Swenor, Jacobs and Dennehy echoed the importance of understanding the challenges and joys faced by people with disabilities.



Dr. John Dennehy

An NIH blog post from 2021 (<https://bit.ly/30muEQo>) cited a publication from the National Center for Science and Engineering Statistics that of all graduates awarded doctoral degrees in the biological sciences in 2019, approximately 9 percent reported having one or more disabilities.

In the words of Swenor, “our choices, the decisions we make, the people we include or exclude, purposefully or not, matter. They have an impact.”

An archived recording is available to NIH staff on the NIAID Diversity and Inclusion channel on Microsoft Stream at <https://bit.ly/3RUg8Cp>.

For information on employee resource groups focused on the interests and quality of life for staff and trainees with disabilities, visit EDI at: <https://>



ON THE COVER: 3D print of hemagglutinin, one of the proteins found on the surface of influenza virus that enables the virus to infect human cells.

IMAGE: NIH

### The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email [nihreford@nih.gov](mailto:nihreford@nih.gov).

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At left, Pathways intern Johnson and his colleagues present their project to an ORS audience. Above, years later, he and his mom Tammie Edwards, also an NIH'er, pose for photos at the NFL draft venue.

director and chief of the Medical Arts Branch in the Office of Research Services and, since May 2021, director of the ORS Division of Amenities and Transportation Services.

“My mom always worked at NIH when I was growing up and I’ve always loved going to work with her, seeing

**NFL**

CONTINUED FROM PAGE 1

National Football League draft. It might have been the childhood dream come true for a lot of youngsters, but Johnson wasn’t exactly thinking that way as a kid.

“I didn’t start playing football until late in high school—my junior year,” said Johnson, who grew up in Bowie, Md. “I worked at NIH and I was more focused on trying to be an engineer.”

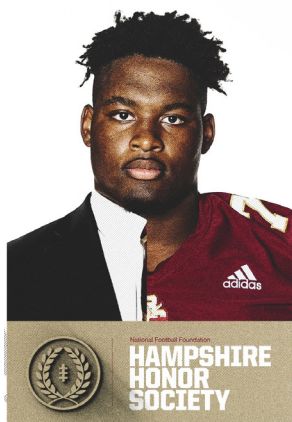
In fact, golf was Johnson’s sport in his early years at Riverdale Baptist School in Upper Marlboro, Md. A bus driver who drove Johnson home every day after golf practice suggested he try football.

“He was always saying, ‘Hey, I think you should try out for football—even if it’s not something that you like or that you get really good at...It’s something that’ll teach you qualities like teamwork and discipline.’ At first, I was skeptical, because I had not played football before and the other guys on the team had a lot more experience.”

Johnson recalled not being a particularly large or strong kid physically. Nor was he consumed with the sport.

“I wasn’t as big as the other guys that played my position,” he said. “But I think [the bus driver] saw something...I had big hands and long arms, so maybe he thought if I could get in the weight room and develop, I could end up being a pretty good football player. I was a fan of the Pittsburgh Steelers. I would watch games, but it wasn’t a big thing in my life.”

The bus driver’s suggestion resonated



with Johnson, but it was another influencer who made the difference.

“Really, it was my mom who pushed me to play,” Johnson recalled. “Over the course of a few days, she basically told me, ‘You should try it, because you don’t want to look back and have regrets.’ And definitely I look back now and I’m glad I made that decision. Because I think I truly would have regretted not taking the chance.”

At first, Johnson didn’t appear to be a natural on the football field.

“I struggled a lot very early on,” he said. “I didn’t really [get into any games] until the end of my junior year. But I really fell in love with it—with the ability to just work hard and do what your coaches said, and ultimately see yourself develop and get better over time.”

At about the same time he was contemplating the jump from golf to the gridiron, Johnson was already mapping out his engineering future.

As a youngster, he had visited NIH with his mom, Tammie Edwards, former creative

how she interacted with her staff,” Johnson remembered. “When I got to eighth grade or so, sometimes I’d come in and help my mom by answering the phones. I always thought that was great because it felt to me like I was doing something productive.”

Years later, Johnson applied for and secured an NIH Pathways Program internship with the Office of Research Facilities. He was assigned first to the Division of Facility Stewardship.

“We would survey buildings, get the dimensions of rooms and build the rent models in AutoCAD,” he explained.

Once he graduated high school and entered Davidson College, intern Johnson moved to ORF’s Division of Technical Resources. There he helped program 10 business intelligence visualization websites for the NIH central utility plant (CUP).

“Intern Zion did an excellent job developing the engineering dashboard, allowing CUP management and engineers to remotely monitor and optimize plant operations,” noted Dr. Don Guan, senior engineer in the division’s Technical Support Branch and Johnson’s supervisor.



Johnson worked at NIH as an intern and played football for two schools during an outstanding college career, which garnered scholastic honors as well as athletic acclaim.

PHOTOS COURTESY TAMMIE EDWARDS

## Schor Selected to Serve as Acting DDIR

NINDS DEPUTY ASSUMES NEW ROLE

Dr. Nina Schor has taken on the role of NIH acting deputy director for intramural research (DDIR) in the Office of the Director. She stepped into the position vacated by Dr. Michael Gottesman, who served as DDIR for 29 years and returned to the NCI Center for Cancer Research, where he is chief of the Laboratory of Cell Biology.

As acting DDIR, Schor leads the NIH Intramural Research Program (IRP) and facilitates coordination and collaboration among the 24 institutes and centers that are a part of the agency's distinct research community. She's responsible for selection and approval of new NIH principal investigators, human subjects research protection,

research integrity, technology transfer and animal care and use for the IRP.

Additionally, Schor will oversee efforts to train the next generation of biomedical and behavioral researchers at NIH, as well as efforts to foster a diverse and inclusive culture across the IRP.

With a career that has touched all realms of the biomedical research enterprise, Schor brings substantial experience as an educator, scientist, clinician and administrator. She joined NIH in January 2018 as deputy director of the National Institute of Neurological Disorders and Stroke. In May 2021, she also assumed the role of acting NINDS scientific director.

As deputy director, Schor guided the institute's strategic planning activities, career devel-

opment programs, maternal and child neurologic health collaborations with other NIH institutes, and the creation and implementation of the Ultra-Rare GENE-based Therapies (URGenT) Network.

Before joining NIH, Schor worked at the University of Rochester, where for nearly 12 years she held the positions of chair of the department of pediatrics and pediatrician-in-chief of the Golisano Children's Hospital.

Prior to that, she spent 20 years building her academic and scientific career at the University of Pittsburgh, culminating with roles as associate dean for medical student research and chief of the division of child neurology in the departments of pediatrics and neurology.

Schor earned her Ph.D. in medical biochemistry from Rockefeller University and her M.D. from Cornell University Medical College. Her residency and postdoctoral fellowship training in pediatrics, child neurology and molecular biochemistry and pharmacology took place at Harvard University Medical School and Boston Children's Hospital, where she began her three-decades-long NIH-funded research efforts focused on targeted therapy for neuroblastoma, a type of pediatric cancer, and neuronal cell death caused by oxidative stress, which occurs when harmful forms of oxygen molecules damage cells.



Johnson said he got his first experience in a computer science environment working as an intern at NIH. He's since earned bachelor's and master's degrees in the field.

"The page that I worked on will show the critical temperature, flow and pressure of the boilers, gas turbine and chillers," Johnson explained. "That's important because workers at home need to be able to see these real-time operational data. If something were to go wrong, they might have to rush in and work at the power plant, even outside of working hours. That was really my first experience in a computer science environment."

After transferring to Boston College to take advantage of both an athletics scholarship offer and the school's reputation for outstanding academics, Johnson graduated in 2020 with a bachelor's degree in computer science. He had been deemed Offensive Linesman of the Week three times and was named to the All-Atlantic Coast Conference team. He completed his final Pathways assignment late that year too, as the world had plunged firmly into pandemic mode.

In 2021, Johnson earned his master's in cybersecurity along with first team All-ACC honors and numerous other academic and sports accolades.

By April 2022, he found himself seated in a deluxe Las Vegas venue, hearing his name called in the first round of the NFL draft and accepting an LA Chargers jersey on live TV.

"I think I still haven't realized it yet because I'm moreso just focused on what's next and what I need to do to sustain myself at the next level," he said. "But it's definitely a story you don't hear very often." **R**



In Lipsett Amphitheater at the first in-person WALs event in 2 years, Dr. Nina Schor introduced the guest speaker. Schor began serving as acting deputy director for intramural research on Aug. 1.

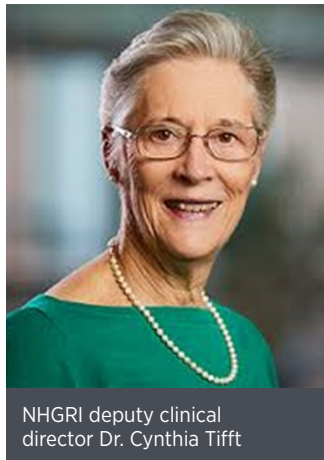
PHOTO: CHIA-CHI CHARLIE CHANG

## Flysjo

CONTINUED FROM PAGE 1

Patients with GM1 and GM2 can't make the enzyme, so their bodies can't degrade the gangliosides.

"Basically, you've got this big fat called ceramide, with sugars that are attached, and there's a specific enzyme that breaks off each sugar," explained Tift. "The first sugar to come off is a galactose. Without the beta-galactosidase enzyme, that first sugar



NHGRI deputy clinical director Dr. Cynthia Tift

[GM1] can't come off and gets stored in the neurons, building up to toxic levels in the brain."

The disorders are recessive. Each parent is an asymptomatic carrier,

giving a copy of the faulty gene to the child. Hampus, Isabella and Julia have the late-infantile subtype of GM1, in which symptoms don't start appearing until 1 to 2 years old.

When Hampus was diagnosed, his sisters were 2 and at the time seemed unaffected. But months later, they too began showing symptoms.

"Genetic testing confirmed our worst fears and our world just fell apart," Niclas said during an NIH Rare Disease Day symposium in 2020. "Our kids were going to lose one another and we were going to lose them all."

### Collaborating toward a therapy

While Tift was researching GM1, a team at the University of Massachusetts was working to develop a gene therapy vector. A group at Auburn University's veterinary program began testing that vector in cats with GM1 after it showed potential in mice.

"Our 3 groups met at a patient advocacy meeting and we worked together for 10 years trying to bring this to fruition—one doing the vector, one doing the large animal testing and us doing the natural history study in the patients, because very little was known about how the disease progresses," Tift said. "And

we cobbled together enough resources to be able to produce the first human-grade batch of gene therapy vector."

Following their children's diagnosis, Niclas and Jessica connected with foundations and began researching online. When they learned of Tift's first-in-human gene therapy trial at NIH, the small study was not yet recruiting patients. As soon as the trial opened in 2019, they applied to enroll their children.

The clinical trial is an intravenous, single administration of a healthy copy of the GLB1 gene. It's an open-label study, meaning no placebos; every child gets the therapy. In May 2019, a 10-year-old girl became the first human to receive the therapy.

### Arriving in the nick of time

The Flysjo family enrolled in the trial and planned to travel to NIH in March 2020. But a call came in the middle of the night, Swedish time. NIH told them to travel immediately. The international border would be closing due to Covid-19.

After reworking their travel plans, which almost got derailed when a hurricane closed the bridge to the airport, the Flysjo family cleared immigration 3 hours before the border closed.

"We then packed our stuff into a rental car with the kids screaming in the background,"



Niclas recalled. "We were so relieved when we finally reached our destination."

After their required 2-week off-site quarantine, Hampus, Isabella and Julia got prepped for treatment. They got dosed on

Apr. 28, 2020, becoming the third, fourth and fifth kids to receive the therapy. Given the children's immunosuppressed state following treatment, and ongoing pandemic travel restrictions, the family stayed at the Children's Inn for 7 months.

### 'The kids look great!'

Back at NIH spring 2022 for their 2-year evaluation, in a room at the Clinical Center, Hampus sat in his stroller and each twin girl on a parent's lap. Hampus and Isabella tugged at a stuffed monkey, a situation they peacefully and quickly resolved when he relinquished it to his sister.

"Parents have said this to me for years—and I've finally come to believe them—that there's a lot more in their [kids'] brains



Isabella (l), Julia and Hampus sit with their parents in their backyard in Sweden.

PHOTO: NICLAS FLYSJO



Isabella, Julia and Hampus by the Children's Inn playground

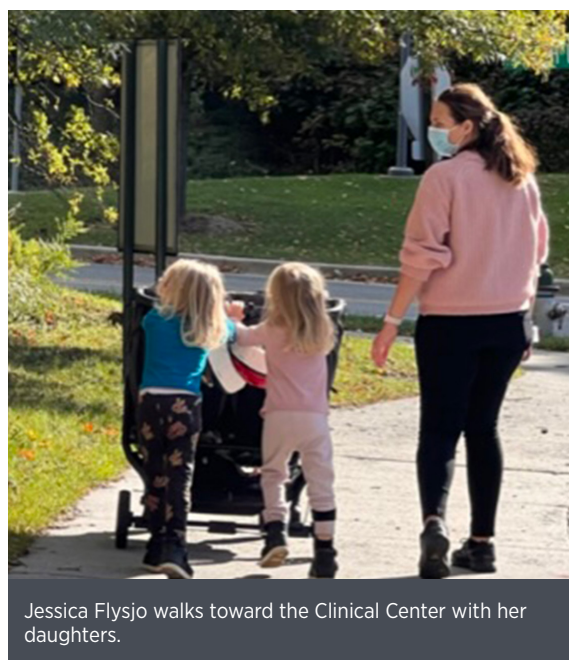
than they can articulate," said Tifft. In GM1 patients, receptive language is good and the children can learn.

The three, sweet young faces looked expectantly at the new visitor in the room interviewing their father. Hampus has some words and can sign, but all three children only understand Swedish.

"It's difficult to teach them new things," said Niclas. "It's extra work for them to learn things that come naturally to other children."

At the follow-up, though, the brain scans and developmental testing showed minimal if any decline since the gene therapy. The kids had not lost any skills.

"We would not have expected that if they



Jessica Flysjo walks toward the Clinical Center with her daughters.

has done well with this vector, but these three children have done exceedingly well. How long that will last, I don't know."

By this age, GM1 patients typically would have difficulty eating, chewing and swallowing, but the Flysjo kids are nowhere near that, said Tifft. "Part of this has to do with the excellent care they receive from their family."

Niclas and Jessica provide a supportive, loving environment and keep the kids active. "We love the outdoors," said Niclas. "In summer, we swim in the ocean. In winter, we play in the snow in the backyard."

Every day, after school, Niclas's parents take the kids for a 2- to 3-mile walk.

"I think half the reason these kids are still walking is not just the therapy," said Tifft, "but because they're out there every day, moving."

The Flysjo parents remain hopeful about the potentially life-saving treatment.

"We knew with Covid, some people were stopping treatments or being sent home as clinical trials were discontinued," said Niclas. "We're so grateful to be able to come here. There's no other place in the world where we could get treatment for this."

The Flysjos have yet another reason to be grateful. Through preimplantation genetics, Jessica had a healthy embryo implanted. They're expecting their fourth child in December. **R**

were not treated," said Tifft. Another surprise was that they had matured, she added. During the latest rounds of testing, they knew the drill, cooperated and were not as needy.

"The kids look great," she said. "Not every child

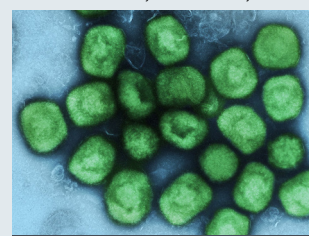
ANOTHER THREAT?

Keeping An Eye on Monkeypox

While much attention remains on the Covid-19 pandemic, another virus is circulating that requires health care providers and the public to stay alert—monkeypox

What is monkeypox?

The monkeypox virus is in the same genus as variola virus (the cause of smallpox). According to the Centers for Disease Control and Prevention, monkeypox is rarely fatal. Initial symptoms include fever, headache, fatigue and swollen lymph nodes, followed by a rash of lesions.



Colorized electron micrograph of monkeypox virus particles (green) cultivated and purified from cell culture

IMAGE: NIAID

How many cases are in the U.S.?

As of July 24, there have been 2,891 confirmed cases of monkeypox across the country.

Monkeypox spreads through direct contact with body fluids or lesions and indirect contact with contaminated clothing or bedding. Animal-to-human transmission can occur through a bite or scratch or contact with body fluids.

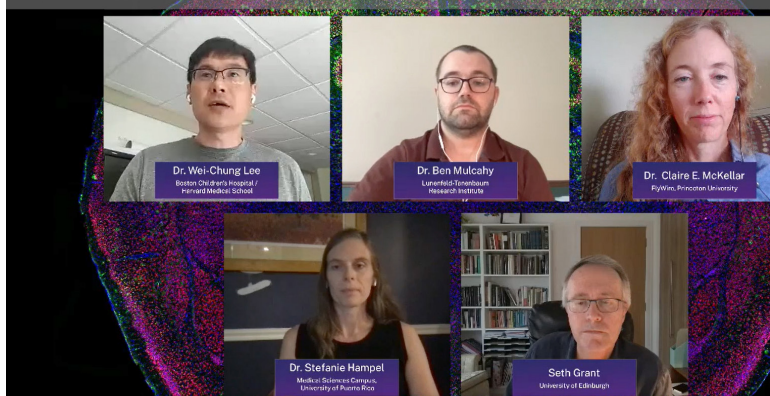
Should we be worried?

"I do not like to use the word worry, because that is an affective response," said NIAID director Dr. Anthony Fauci during a recent interview with the *NIH Record*. "I think you should be paying attention to it, take it very seriously and don't underestimate it. That is one of the problems you get into when dealing with emerging infectious diseases. When you do not take it seriously enough, you can be poorly prepared."

Fortunately, "we do have countermeasures," said Fauci, who urges health officials to stay informed and be proactive. There is an FDA-approved vaccine—Jynneos—that can be used pre- and post-exposure, and an antiviral that can help treat monkeypox infections.

With monkeypox, the message is clear: Be prepared; stay vigilant. "We should be doing a lot more testing," Fauci advised, "and ramp up the availability of countermeasures for it."

## Advancing our Understanding of the Brain and Behavior Through Connectomics



Participants in BRAIN's connectomics session shared progress in the field and how tools, platforms and analyses can inform study of circuits from sensory processing to the control of behavior.

## BRAIN Convenes to Discuss Open Science, New Tools

BY SHANNON E. GARNETT

The Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative hosted its 8th annual meeting, Open Science, New Tools, on June 21-22. Marking its third year in an all-virtual format, the gathering brought together more than 2,600 participants—federally funded scientists, leaders and staff, as well as non-federal organizations, researchers interested in joining the BRAIN community, media and the public.

“The purpose of this open meeting is to continue to build the brain community and provide a forum for discussing exciting new scientific developments and potential new directions and to identify areas of collaboration and research coordination,” said NIH BRAIN director Dr. John Ngai.

The 2-day conference featured plenary lectures, trainee award highlight talks and symposia spanning a range of topics from neuroimmune interactions, neural dynamics of memory formation and rewiring of neural circuitry, to sessions covering the ethical, legal and societal implications of neurotechnologies, to diversity and inclusion opportunities and challenges of human neuroimaging research.

The meeting also included presentations on BRAIN Initiative Cell Census Network resources, understanding mechanisms driving internal states and new tools to track and interpret behavior.

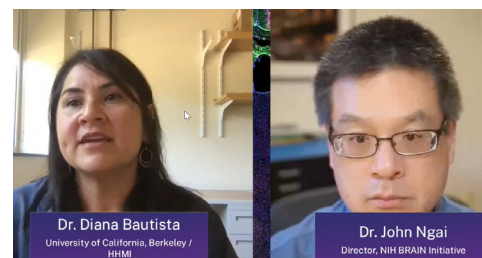
In a session organized by the International Neuroethics Society, BRAIN-funded scientists shared

experiences collaborating. Another interactive talk hosted by the International Neuroinformatics Coordinating Facility focused on resources such as training, career development and best practices for FAIR (findable, accessible, interoperable, reusable) neuroscience research.

New to the gathering this year: BRAIN researchers used a platform called Zohuddle to connect with each other, expand their networks and develop new collaborations at the “Neuroscientist Speed Dating” event. Meeting attendees also got a chance to

watch and discuss the award-winning film *The Brain Mappers*, which told the story of research teams involved in whole brain connectomics and included first-person accounts from scientists who engaged early in the BRAIN Initiative.

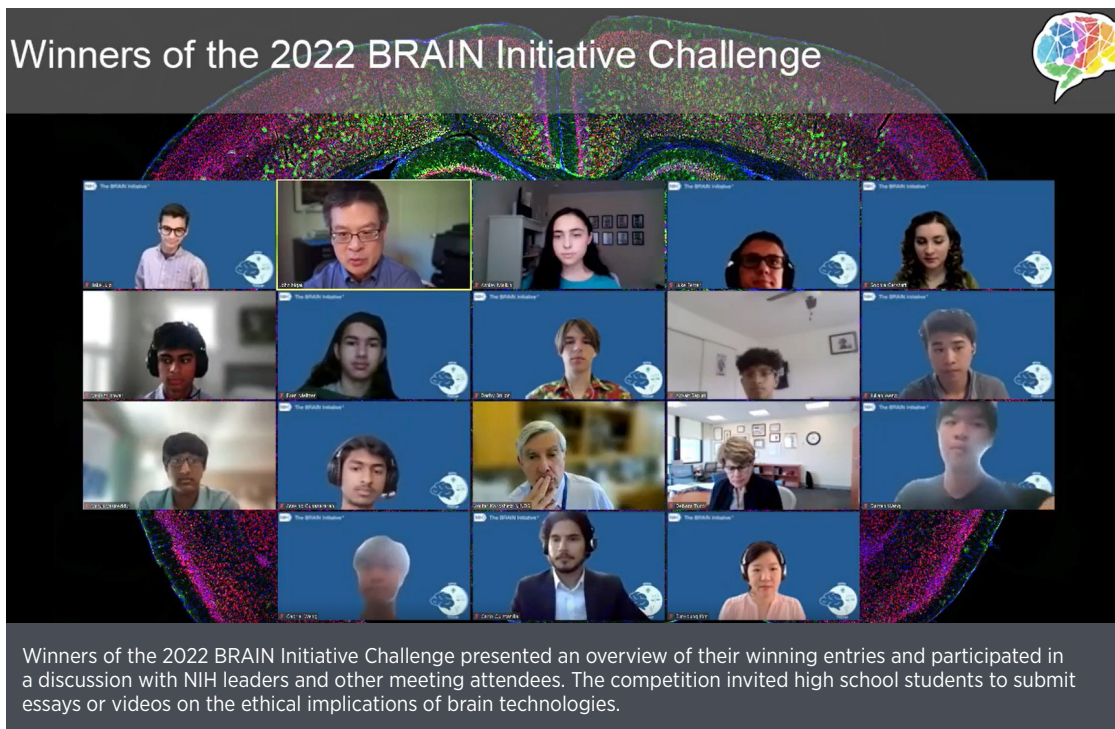
On day one, Ngai joined with NIDCD director Dr. Debara Tucci, NIA director Dr. Richard Hodes and NINDS director Dr. Walter Koroshetz to announce winners from the BRAIN Initiative Challenge. This federal competition encouraged U.S.



The BRAIN meeting kicked off with a session titled “Peripheral Neuroimmune Interactions Drive Itch and Inflammation” by Dr. Diana Bautista of the Helen Wills Neuroscience Institute at the University of California, Berkeley. NIH BRAIN Initiative director Dr. John Ngai introduced the speaker.

high school students from all backgrounds to submit essays or videos on the ethical implications of current and developing brain technologies.

Winners presented an overview of their



Winners of the 2022 BRAIN Initiative Challenge presented an overview of their winning entries and participated in a discussion with NIH leaders and other meeting attendees. The competition invited high school students to submit essays or videos on the ethical implications of brain technologies.



entries, shared their main ethical concerns and participated in a lively discussion with NIH leaders and other meeting attendees.

View the winning entries at: <https://www.challenge.gov/?challenge=brain-initiative-2022&tab=winners>.

Throughout the meeting, participants were able to interact via Q&A sessions and the web platform's messaging feature, explore more than 400 interactive posters in the iPosters gallery and chat with the presenters and visit a selection of virtual exhibit booths.

Posters, exhibit materials, broadcasts and resources are available on-demand and at no cost through June 2023 at <https://eventmobi.com/brainmeeting2022/>.

### Winners of the 2022 'Show Us Your BRAINS!' Contest Announced

Winners of the "Show Us Your BRAINS!" photo and video contest were announced on the second day. The contest showcases cool, eye-catching images and videos—some using technologies that were developed with BRAIN Initiative support.

Photo winners include:

- 1st Place: "The Intersection of Memory and Memory" by Stephanie Grella, Boston University. Two memories captured under the microscope. Peering into the hippocampus of a mouse using viral technology and optogenetics.

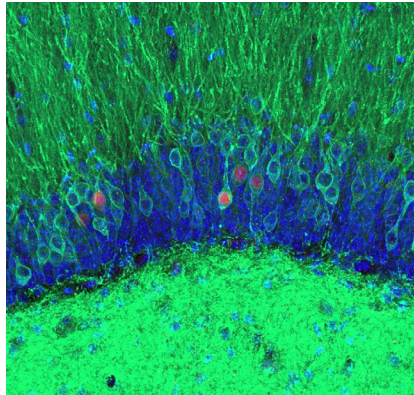
- 2nd Place: "Mindmap—The Intricate Wiring of the Human Brain" by Sahar Ahmad, Ye Wu and Pew-Thian Yap, University of North Carolina at Chapel Hill. Brain activity is orchestrated by propagating information between brain regions through Fiber tracts, visualized via diffusion MRI tractography.

- 3rd Place: "Zebrafish Brain Thinking Abraham Lincoln" by Esengül Öztürk, Çanakkale Onsekiz Mart University. Image taken from a zebrafish brain tissue section, synaptophysin as the primary antibody, Alexa 555 and DAPI as secondary antibody, and looks like Abraham Lincoln's side profile.

To view the full group of winning images and videos, visit: <https://braininitiative.nih.gov/news-events/show-us-your-brains-photo-video-contest>.

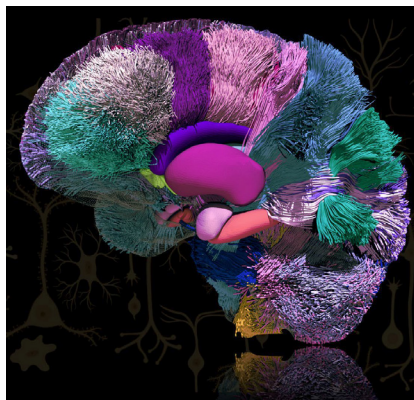
Launched in 2013, BRAIN is a large-scale effort funded by NIH, other government agencies and private organizations to revolutionize our understanding of the human brain.

A major goal of the BRAIN Initiative is to encourage researchers and organizations from diverse disciplines to work together. The annual meetings are an important part of this effort. 



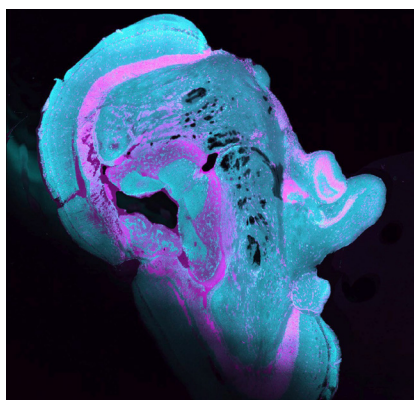
1st place "The Intersection of Memory and Memory"

IMAGE: STEPHANIE GRELLA



2nd place "Mindmap—The Intricate Wiring of the Human Brain"

IMAGE: SAHAR AHMAD, YE WU, PEW-THIAN YAP



3rd place "Zebrafish Brain Thinking Abraham Lincoln"

IMAGE: ESENGÜL ÖZTÜRK

### Participants Needed for Nipah Vaccine Study

VRC researchers seek healthy volunteers 18 to 60 years old to participate in an investigational vaccine targeting the Nipah virus. There is no Nipah virus in the vaccine, so there is no risk of infection. Financial compensation provided. For more information, call (866) 444-2214, email [ccopr@nih.gov](mailto:ccopr@nih.gov) or visit <https://go.usa.gov/xSrPw>.

### New Flu Vaccine Study Seeks Volunteers

Healthy adults ages 18-55 are needed for an influenza (flu) vaccine study. The flu is a respiratory virus that affects people of all ages. NIH researchers are studying a new flu vaccine that may protect against different flu strains. If you are healthy and interested in helping fight the flu, consider joining a research study that aims to learn more about the safety of this vaccine.

There is no cost to participate and compensation is provided. For more information, call (866) 444-2214 (TTY users dial 711) or email [ccopr@nih.gov](mailto:ccopr@nih.gov) and refer to study #000320-1. Online: <https://go.usa.gov/xeR5P>.

### Diet and SCD Study Seeks Adults

Does diet affect sickle cell disease (SCD)? Clinical Center researchers are conducting a study to help discover the answer. The study will examine the impact of diet and nutrition on the health of adults living with SCD. If you are age 18 years or older, diagnosed with SCD and wish to participate, contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email [ccopr@nih.gov](mailto:ccopr@nih.gov). Refer to study #000518-CC. Online: <http://go.usa.gov/xzFeR>.

### CLL Study Recruits

NHLBI researchers are looking for people ages 18 and older who have chronic lymphocytic leukemia (CLL) that has progressed after first-line treatment. Patients will be treated at NIH for the duration (typically 5 weeks) of the ramp-up phase of venetoclax and will then be transitioned to the care of their local hematologist/oncologist for continual treatment. The trial aims to study changes in the genetic makeup of CLL during the early phase of treatment with venetoclax. There is no charge for study-related tests, medications or procedures. Travel assistance may be provided. For more information about study #19-H-0111, call: (866) 444-2214 (TTY users dial 711). Online: <https://go.usa.gov/xyrqb>.

### Volunteer to Give Blood Samples

NHLBI researchers seek healthy volunteers to provide blood samples for research studies of blood vessels and immune diseases that cause clotting. In this study, investigators want to understand the basis of these diseases to facilitate development of better treatments. Compensation provided. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or [ccopr@nih.gov](mailto:ccopr@nih.gov). Refer to study #000829-H Online: <https://go.usa.gov/xJDNZ>.

## Long Covid

CONTINUED FROM PAGE 1

of the VA St. Louis Health Care System's Research and Development Service. Long Covid's impact on disability and life expectancy rates and educational attainment in children "will have broad economic and social implications."

"Long Covid" is an umbrella term for the lingering effects that result from a Covid-19 infection. It's a multifaceted disease that can affect nearly every organ system, including the heart, brain and kidneys. Al-Aly estimates between 4 and 7 percent of patients who recover from the initial infection develop the condition. In total, there are about 30 clinical disorders that comprise long Covid. (NIH refers to the condition as Post-Acute Sequelae of SARS-CoV-2 infection.)

Al-Aly first became aware of the existence of long-term complications of SARS-CoV-2, the virus that causes Covid-19, after reading a *New York Times* op-ed article by Fiona Lowenstein. She detailed her prolonged recovery from the virus in April 2020. Shortly after, Al-Aly saw self-reported surveys from patient-led groups suggesting



***"Long Covid is not a monolithic entity. It does not all behave in the same way."***

—DR. ZIYAD AL-ALY



that weakness, fatigue, brain fog and muscle pain were common.

"We asked the simple question, 'What is long Covid?'" said Al-Aly. "We took a high-dimensional approach to leave no stone unturned and characterize the post-acute sequelae of Covid-19."

Very early in the pandemic, he turned to the U.S. Department of Veterans Affairs' electronic health care records—"an amazing and wonderful nationally integrated electronic health record system"—to shed light on the risks of long Covid. His team followed almost 74,000 veterans who had a Covid-19 infection for at least 6 months. He compared them with a group who did not have the virus.

His team found veterans who had Covid-19 were at increased risk for heart disease, diabetes, mental health conditions,



Between 4 and 7 percent of patients who recover from the initial Covid-19 infection develop long Covid, Al-Aly estimates.

IMAGE: NIAID

kidney disease and nervous system disorders such as stroke, headaches and brain fog, and several other problems.

Even a year after publishing his initial results, Al-Aly said the "breadth of organ dysfunction" experienced by people with Covid-19 remains "really jarring."

The risk for developing conditions associated with long Covid was evident even in patients with asymptomatic or mild cases, he said. The risk was even higher in patients who were hospitalized and highest in patients admitted to intensive care.

The individual conditions that make up long Covid do not behave in the same way across age, race or baseline health status.

"Long Covid is not a monolithic entity. It does not all behave in the same way," he noted. Some conditions, for example, occur more often in males and others occurred more often in females. However, the burden of risk was consistently higher in patients with severe Covid-19.

Al-Aly is most concerned about cardiovascular disorders, diabetes, kidney disease and neurologic and mental health disorders because these are chronic conditions that will last a lifetime and affect quality of life and life expectancy.

His team found that people with Covid-19 had an increased risk of several cardiovascular diseases, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and

thromboembolic disease. Patients with mild cases of Covid-19 had the lowest risk of developing one of these conditions.

The team also observed patients with the infection had an increased risk for diabetes within a year of being diagnosed with the virus.

"One to 2 percent who were exposed to SARS-CoV-2 might go on to develop diabetes," Al-Aly said. "It's easy for us to see it in a very large, big-data approach. But it's much harder to see it in the clinics on the frontline."

The pandemic has been a stressful and challenging time for many people. However, those who survived Covid-19 have a significantly higher chance of developing mental health problems—anxiety disorders, depression, substance use disorders and sleep disorders. In many cases, these patients were prescribed antidepressants, such as SSRIs and benzodiazepines.

Alarmingly, some patients with long Covid have returned to the clinic seeking pain relief. "We've seen early signals in our data—which I hope does not continue—of a resurgence of opioid use, specifically in people with SARS-CoV-2 infection," Al-Aly warned. "That demands our attention to nip it in the bud."

Vaccination against Covid-19 reduces the risk of long Covid, but not by much, he noted. People with breakthrough infections had 15 percent less risk of getting the condition. The risk reduction was most clear for blood clots and pulmonary sequelae.

"The best way to prevent long Covid is to prevent Covid in the first place," he said. "If you haven't encountered Covid yet, really, by all means, do your best to prevent yourself and your loved ones from having it."

Long Covid is not rare, he said. Addressing the challenges posed by long Covid will require an urgent response from governments and health care systems. They must adapt quickly and establish post-Covid care strategies.

Al-Aly concluded by highlighting the role patients have played.

"My team would not be researching long Covid were it not for the wonderful patient advocacy groups who gave us strength and warmth in our hearts to pursue this," he said. "This has been a challenging journey. Had it not been for them we would not be here." **R**

## Vaccine-Induced Immunity to Omicron Wanes Over Time

New clinical trial data reveals that while Covid-19 booster vaccinations in adults elicit high levels of neutralizing antibodies against the Omicron variant of SARS-CoV-2, antibody levels decrease substantially within 3 months. The findings, published in *Cell Reports Medicine*, are from a study led by NIAID's Infectious Diseases Clinical Research Consortium.

As part of a "mix and match" clinical trial, investigators administered Covid-19 booster shots to adults in the U.S. who had previously received a primary Covid-19 vaccination series. Some participants received the same vaccine as their primary series; others received a different vaccine. Investigators then evaluated immune responses over time.

In the new analysis, investigators found nearly all vaccine combinations evaluated elicited high levels of neutralizing antibodies to the Omicron BA.1 sub-lineage. Immune responses to Omicron in all groups waned substantially, with neutralizing antibody levels decreasing 2.4- to 5.3-fold by 3 months post-boost.

Omicron sub-lineages BA.2.12.1 and BA.4/BA.5 were 1.5 and 2.5 times less susceptible to neutralization, respectively, compared to the BA.1 sub-lineage, and 7.5 and 12.4 times less susceptible relative to the ancestral D614G strain. BA.5 currently is the dominant variant in the U.S.

Additionally, the immune response to Omicron sub-lineages show reduced susceptibility to these rapidly emerging subvariants. The data could be used to inform decisions regarding future vaccine schedule recommendations, including the need for variant vaccine boosting.

## Preterm Birth More Likely with Exposure to Phthalates

Pregnant women who were exposed to multiple phthalates during pregnancy had an increased risk of preterm birth, according to new research by NIH. Phthalates are chemicals used in personal care products, such as cosmetics, as well as in solvents, detergents and food packaging.

After analyzing data from more than 6,000 pregnant women in the U.S., researchers found that women with higher concentrations of several phthalate metabolites in their urine were more likely to deliver their babies preterm, which is delivering 3 or more weeks before a mother's due date.

"Having a preterm birth can be dangerous for both baby and mom, so it is important to identify risk factors that could prevent it," said Dr. Kelly Ferguson, an NIEHS epidemiologist and senior author on the study, published in *JAMA Pediatrics*.

In the study—the largest to date on this topic—Ferguson and her team pooled data from 16 studies



A pregnant woman may be exposed to phthalates by eating packaged foods and beverages or using personal care products.

IMAGE: NIEHS

conducted across the country that included individual participant data on prenatal urinary phthalate metabolites (representing exposure to phthalates) as well as the timing of delivery. Researchers analyzed data from pregnant women who delivered between 1983-2018. Nine percent, or 539, of the women in the study delivered preterm. Phthalate metabolites were detected in more than 96 percent of urine samples.

Higher concentrations of most phthalate metabolites examined were associated with slightly higher odds of preterm birth. Exposure to 4 of the 11 phthalates found in the pregnant women was associated with a 14-16 percent greater probability of having a preterm birth. The most consistent findings were for exposure to a phthalate that is used commonly in personal care products like nail polish and cosmetics.

The researchers also used statistical models to simulate interventions that reduce phthalate exposures. They found that reducing the mixture of phthalate metabolite levels by 50 percent could prevent preterm births by 12 percent on average.

Interventions targeting behaviors, such as trying to select phthalate-free personal care products (if listed on label), voluntary actions from companies to reduce phthalates in their products or changes in standards and regulations could contribute to exposure reduction and protect pregnancies.

"It is difficult for people to completely eliminate exposure to these chemicals in everyday life, but our results show that even small reductions within a large population could have positive impacts on both mothers and their children," said Dr. Barrett Welch, a postdoctoral fellow at NIEHS and first author on the study.

Eating fresh home-cooked food, avoiding processed food that comes in plastic containers or wrapping and selecting fragrance-free products or those labeled "phthalate-free," are examples of things people can do that may reduce their exposures.

## New Clue into How Exercise Influences Body Weight

Physical activity leads to many molecular changes in the body, but it remains unclear how exercise protects against obesity at a molecular level.

A team of researchers led by Drs. Yong Xu at Baylor College of Medicine and Jonathan Long at Stanford University analyzed blood samples taken from mice before and after intense running on a treadmill. The scientists looked for compounds in blood plasma with higher levels after exercise. The study, partly funded by NIH, appeared in *Nature*.

The team found that the largest exercise-induced increase was in a compound called N-lactoyl-phenylalanine, or Lac-Phe. The team found a similar increase in Lac-Phe after exercise in blood samples from thoroughbred racehorses. They also analyzed blood samples from people and found increases in Lac-Phe after various types of exercise. These findings suggest that the exercise-induced increase in Lac-Phe likely occurs across mammals.

When mice were fed a high-fat diet, injecting a



PHOTO: NEW AFRICA/SHUTTERSTOCK

large dose of Lac-Phe reduced food intake by about half over 12 hours even though blood Lac-Phe levels fell back to baseline level within an hour. Lac-Phe treatment did not affect the mice's movement or energy

expenditure. Obese mice treated with Lac-Phe daily for 10 days lost weight compared to control mice. This was due to a decrease in body fat. Obese mice treated with Lac-Phe also had lower blood glucose levels than control mice. Lac-Phe treatment, in contrast, did not affect food intake in lean mice eating a normal chow diet.

"Regular exercise has been proven to help weight maintenance, regulate appetite and improve the metabolic profile, especially for people who are overweight and obese," Xu said. "If we can understand the mechanism by which exercise triggers these benefits, then we are closer to helping many people improve their health."

"Our next step," said Long, "is to identify the brain Lac-Phe receptor in order to understand how Lac-Phe suppresses feeding and obesity."—adapted from *NIH Research Matters*

## TALENT BEYOND THE BENCH NIH Fellows Make Plushies for Patients

Two fellows in Dr. Charles Venditti's lab spent many hours over several months crocheting what they're calling Pam and Pauline's Plushies for Patients.

"These are the coolest handmade stuffed animals I have ever seen," said Venditti, a senior investigator in NHGRI's Metabolic Medicine Branch.

Dr. Pam Head, an NIGMS postdoctoral research associate (PRAT) fellow, and Pauline Hoffman, an NHGRI postbac IRTA fellow, made 35 unique plushies for children who were stuck indoors at a medical conference in Bethesda over a weekend in June. The conference was for families grappling with MMA (methylmalonic acidemia), PA (propionic acidemia) and cobalamin deficiencies—rare, genetic metabolic disorders.

Head began crocheting in graduate school to pass the time during lectures. She started making stuffed animals earlier this year as gifts for colleagues returning to the office. When NHGRI clinical investigator Dr. Irini Manoli saw them, she asked whether Head would share a couple with patients visiting the Clinical Center. When she did, the patients' eyes lit up, recalled Manoli. "It was most heart-warming," she said.

With the summer family conference in mind, Head then teamed up with Hoffman and the two set to work during off-hours—on weekday evenings and weekends—to prepare one for each child attending the meeting.

"I became not just Pauline's mentor in the lab but also in crocheting," said Head.

"It was such a special set of gifts," said Venditti, who has devoted his career to studying organic acidemias. "All the kids got to pick one and even some of the unaffected siblings got plushies as well."

MMA and PA are life-threatening conditions that cause frequent hospitalizations and long-term complications such as learning and vision problems. While cobalamin (vitamin B12) injections can help milder forms, treatment largely consists of managing symptoms and, for some patients, organ transplants. Venditti's team focuses on developing genomic therapies for these disorders.

At the conference, the parents appreciated the plushies that brought their children joy and served the dual purpose of keeping their kids occupied so they could focus on the lectures.

"I hope the person who made them knows how happy the kids were to receive them," said Misty Garcia, whose daughter received a llama plushie.

Head and Hoffman said they hope to make more plushies in the future to donate to other young patients. —**Dana Talesnik**



Above, Grayson Parke, age 3, snuggles with his snake plushie. Below, Stephanie Evans poses with Dr. Charles Venditti and the dog and duck plushies she received. "She would not put them down," said Venditti." Same goes for the other kids.



At left, NIGMS postdoc fellow Dr. Pam Head poses with the plushies she crocheted for young people with MMA, PA and other cobalamin disorders. Sacha George (c), 8, who has cobalamin C deficiency, hugs his plushie. At right, Pauline Hoffman, an NHGRI postbac IRTA fellow, holds up a plushie she crocheted.