

## Advances in Care Help Save Young HLRCC Patient

BY DANA TALESNIK

When college student Andrew Lee was diagnosed with stage 4 rare kidney cancer in 2015, he would spend the next 4 years fighting it. He knew he might succumb to his illness but hoped his efforts would one day prevent others from suffering. Lee lost his battle in 2019, yet his legacy lives on.

The research Lee enabled—having participated in 7 NIH-led clinical trials, donated living tissue and raised nearly \$500,000 for rare kidney cancer studies—is already saving lives. One lucky patient is 20-year-old Luke Schmaedeke.

Schmaedeke had known for several years that he could have a syndrome called

hereditary leiomyomatosis and renal cell cancer (HLRCC). Patients with HLRCC are at risk for developing benign renal cysts which, in some patients, lead to the aggressive, lethal form of kidney cancer that took Lee's life.

In November, at Schmaedeke's first MRI screening for kidney cancer at the Mayo Clinic, doctors found a small, worrisome mass.

"My anxiety levels started going up," said Jen Schmaedeke, Luke's mother, speaking from the family's home in Minnesota. "We were in shock because here's this thing



Luke Schmaedeke, 20, had a partial nephrectomy at NIH.

SEE HLRCC, PAGE 6



Mid-summer Santa visit to Inn? See story, p. 12.

### ALSO THIS ISSUE

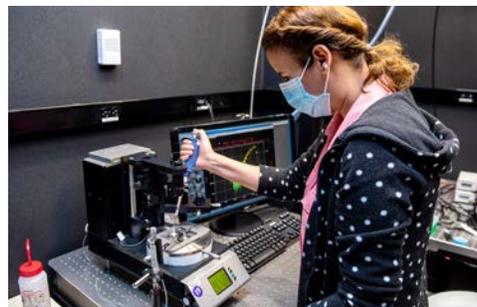
|  |    |
|--|----|
| Surgeon General Talks About Social Connections Amid Pandemic . . . . . | 3  |
| NCI Reports Declining Cancer Death Rates . . . . .                     | 5  |
| Digest . . . . .   | 10 |
| Milestones . . . . .   | 11 |
| Seen . . . . .   | 12 |

## PIVOTING WITH PATIENCE Neuman Lab Looks to Examine Coronavirus Inhibitors

BY CARLA GARNETT

Since 2006, Dr. Keir Neuman, senior investigator in NHLBI's Laboratory of Single Molecule Biophysics, has studied enzymes—specifically ones that control or manipulate the structure of DNA. His group has had enormous success with two in particular—topoisomerases, which untwist and untangle DNA, and helicases, which unwind the double helix.

Pre-Covid and extreme telework, you could find several members of the team in the ultra-quiet darkness of a custom-designed lab, specially calibrated for light,



Dr. Hajnalka Harami-Papp in NHLBI's Laboratory of Single Molecule Biophysics

PHOTO: NIH OFFICE OF HUMAN RESOURCES

sound and motion. Scientists who came to biology by way of physics, they might look like they are adding super-tiny Lego pieces to a desk-size 3-D puzzle. In a sense, they are.

"We're trying to measure the motion of

SEE PIVOT, PAGE 4

This article begins a special series on pandemic pivots—intramural scientists and labs that changed course to tackle Covid-related research.

## BRAIN Initiative Scientists Gather Virtually

BY SHANNON E. GARNETT

More than 3,500 supporters of the U.S. BRAIN Initiative—including scientists, federal staff and leadership, nongovernmental organizations, media and the



NIH BRAIN Initiative director Dr. John Ngai

PHOTO: BRITTANY HOSEA-SMALL

public—gathered virtually June 15-17 for the 7th annual BRAIN Initiative Investigators Meeting.

"We're calling this meeting virtual

but hopefully we are coming out of this long, dark tunnel," said NIH BRAIN Initiative director Dr. John Ngai, referring to the Covid pandemic that caused the conference to be

SEE BRAIN, PAGE 8

## RFI Issued to Identify Gaps in Women's Health Research

Due Sept. 15

A recent request for information (RFI) from NIH invites comments and testimonies from the extramural scientific community, professional societies and the public to help identify gaps in women's health research.

Responses to this RFI will inform a women's health consensus conference in October 2021. This conference will involve members of NIH and Congress and will address research efforts in three specific areas: rising maternal morbidity and mortality rates, increasing rates of chronic debilitating conditions in women and stagnant cervical cancer survival rates. Conference participants will assess the current state of NIH-supported women's health research, delineate research gaps and identify research opportunities.

RFI responses are due by Sept. 15. For more information and to submit comments, go to <https://www.federalregister.gov/documents/2021/07/01/2021-14151/request-for-information-inviting-comments-to-inform-the-womens-health-consensus-conference-whcc>.

## NIH'er Named Finalist for 2021 Trailblazer Prize

The Foundation for the NIH has selected NIAID's Dr. Ian Myles as one of the finalists for the 4th annual Trailblazer Prize for Clinician-Scientists.

Myles is chief of the epithelial therapeutics unit in NIAID's Laboratory of Clinical Immunology and Microbiology. He was selected by a jury of distinguished biomedical research leaders for his exploration of the skin condition atopic dermatitis, allergy and microbial dysbiosis—an imbalance of the body's microbial communities that cause inflammation—leading to the development of the first in-human trial of topical microbiome transplantation using *Roseomonas mucosa* in treating atopic dermatitis.



The other finalists are Dr. Courtney DiNardo of the University of Texas MD Anderson Cancer Center and Dr. Piro Lito of Memorial Sloan Kettering Cancer Center and Weill Medical College of Cornell University.

"It is thrilling to watch clinician-scientists, early into their careers, dive wholeheartedly into solving biomedical puzzles such as these," said FNIH president and executive director Dr. Maria Freire. "By channeling their passion, intelligence and drive, these finalists have made discoveries that moved science many steps along the path toward better therapeutics and healthier populations. All three

have already had substantial impact in their areas of expertise and we anticipate even greater work from them in the future."

The winner will be announced and awarded the Trailblazer Prize and a \$10,000 honorarium at the 2021 FNIH Awards Ceremony on Wednesday, Oct. 20. For details, visit <https://fnih.org/our-programs/fnih-awards-ceremony>. For more information about the prize, visit <https://fnih.org/our-programs/fnih-trailblazer-prize-clinician-scientists>.

## Nominations Open for Disability Employment Awareness Awards

Due Aug. 13

In October, NIH will observe National Disability Employment Awareness Month (NDEAM). This year's theme is "Accessibility Now and Always." In preparation for the observance of NDEAM at NIH, the Office of Equity, Diversity and Inclusion is seeking nominees for the 3rd annual Cultivating Inclusion: Honoring NIH Champions and Allies of Disability Award ceremony.

Nominees should be individuals who, throughout their NIH career, have made exceptional strides toward the advancement of people with disabilities in our community or that help make NIH a more accessible environment for individuals who have a disability. The award is open to all NIH federal employees and fellows, past or present.

To nominate an individual or group for an award, submit your nomination at [https://nihedi.iad1.qualtrics.com/jfe/form/SV\\_1TirLFihJ5UU14p](https://nihedi.iad1.qualtrics.com/jfe/form/SV_1TirLFihJ5UU14p) by Friday, Aug. 13.

NDEAM was established in 1988 by Congress to educate the American public about disability employment and the varied contributions of American workers with disabilities.

## Blood, Platelet Donations Needed

During the pandemic, the NIH Blood Bank is open Monday through Friday from 7:30 a.m. to 4 p.m. for donations by appointment only. The Donor Center at Fishers Lane is open for platelet and double red cell donations.

Call (301) 496-1048 or email [nihbloodbank@mail.cc.nih.gov](mailto:nihbloodbank@mail.cc.nih.gov) to donate blood at the main campus site and (301) 496-4321 to donate platelets or double red cells in Rockville.

## Annual Food Drive Accepting Online Donations

NIH is participating in the Feds Feed Families virtual summer food drive now through Tuesday, Aug. 31. Federal agencies can help fight hunger in their communities. The campaign will again be run entirely online with three ways to contribute and track donations. The Office of Research Services is NIH's sponsoring organization. For more information, visit <https://www.ors.od.nih.gov/FedsFeedFamilies/Pages/default.aspx>. Email questions about the campaign to [FedsFeedFamiliesNIH@nih.gov](mailto:FedsFeedFamiliesNIH@nih.gov).



## Siblings Perform at CC

Siblings Kenneth and Noelle Naito perform a concert at the Clinical Center on July 8. Noelle is 19 and Kenneth is 21. Playing the violin since the age of 4 and a recent student at the Juilliard School, Kenneth has appeared in many venues throughout the world and frequently performs for a CC audience.

PHOTO: DEBBIE ACCAME

## 2021 Anti-Harassment Training Launched Online, Must Be Taken by Nov. 30

As part of its continued commitment to achieving a harassment-free work environment, NIH recently launched 2021 anti-harassment training. The goals are to educate individuals in the workplace to prevent harassment; raise awareness of what constitutes harassment and the consequences of harassing behavior; and stamp out instances where harassing behavior may exist.

The online training is mandatory and replaces the No FEAR and Prevention of Sexual Harassment training.

All NIH federal employees, trainees, fellows and contractors are required to take the training annually. The 2021 training must be completed by Nov. 30. New hires must complete it within 90 days of onboarding. Failure to comply with the training will result in disablement of a person's active directory accounts until the requirement is met. If your active directory account is disabled, you will be unable to sign into your computer or access emails.

To learn more about EEO mandatory training, visit the Office of Equity, Diversity and Inclusion website at <https://www.edi.nih.gov/training/mandatory-training>.

## Social Connections Key to Fighting Opioid Epidemic

BY ERIC BOCK

The opioid epidemic was swept off the front pages as media focus shifted to the Covid-19 pandemic, said U.S. surgeon general Dr. Vivek Murthy.

“But the struggles have not disappeared,” he added during a virtual conversation with NIH director Dr. Francis Collins at the second annual HEAL Initiative investigator meeting. There were more than 92,700 overdose deaths between Nov. 2019 and Nov. 2020.

Loneliness and perceived social isolation challenge people struggling with addiction, including opioid use disorder. When he first became surgeon general in 2015, Murthy met people throughout the country struggling with loneliness and isolation and he commonly met patients with opioid use disorders who were alone.

Loneliness is a risk factor for mental and physical health conditions, opioid use disorder and addiction relapse, he said. It’s now found to increase the risk of anxiety, depression and cardiac disease.

“Addressing loneliness is an important public health issue if we care about addiction, mental health and the physical well-being of people,” he said.

The pandemic has been a particularly isolating time for adolescents and young adults. Even before the pandemic, many young adults reported high levels of anxiety and depression.



Murthy, during a virtual conversation with NIH director Dr. Francis Collins, at the second annual HEAL Initiative investigator meeting

When it comes to loneliness, what matters most is the quality—not the quantity—of human connections, Murthy said.

“For many young people that I spoke to while traveling across the country, they would say that, ‘yes, we’re connected to people all the time. But we don’t necessarily feel like we can always be ourselves in our social media environment.’ That’s where comparison culture is at its height,” Murthy explained.

Social connections are important sources of resiliency. Many people instinctively reach out to



U.S. surgeon general Dr. Vivek Murthy recently said, “I think the pandemic has accelerated our adoption of telemedicine by perhaps 5, 7 years.”

family members or close friends during difficult times.

“If we want to build a society that’s healthier mentally and physically, that is more resilient and that is also more happy and fulfilled, then we have to think about how we build a society that is more centered around human connection and around relationships,” he said.

The pandemic has made it harder to get treatment for opioid use disorder. One silver lining from the health crisis has been telemedicine. It has the potential to improve and extend access to services for people living with opioid use disorders.

“I think the pandemic has accelerated our adoption of telemedicine by perhaps 5, 7 years,” he said. “We have to sustain that with not only the investment in broadband infrastructure but also with other tools so that people can use it

everywhere,” such as health care reimbursement.

Even though it’s a medical condition, there’s still a stigma around addiction. People who feel judged for their disorders won’t feel comfortable seeking treatment, Murthy explained.

A few years ago, he met a couple who lost their son to an overdose. They told him that whenever they struggled, their friends dropped off food or visited them. When their son died, however, no one stopped by.

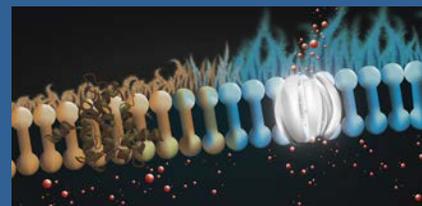
“We still have many people in the country who feel

the shame of what they’re dealing with,” Murthy said. “We still have many family members who feel that this is a source of shame to have a loved one struggling with a substance use disorder.”

He called on society to think about strength differently. Strength isn’t being the most aggressive or loudest, he noted. Rather, strength is “displayed in moments of vulnerability when people have the courage to open up and be themselves,” and it’s “defined by the people who have the courage to display love, patience and compassion, especially when it’s difficult.”

People struggling with opioid use disorders need medication and assisted treatment, counseling and social and recovery services.

“But the engine that will drive our healing is fundamentally the love and compassion that come from human relationships,” Murthy concluded. **R**



ON THE COVER: *New approach shows promise for treating cystic fibrosis. In people with cystic fibrosis, a protein that releases a key infection-fighting agent (red spheres), is missing or defective (brown ribbon). Amphotericin (white structure) can form channels to release bicarbonate, restoring the antibiotic properties of the airway surface liquid, which plays a key role in maintaining lung health.*

IMAGE: REBECCA SCHULTZ, CARLE ILLINOIS COLLEGE OF MEDICINE

### 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 [nihrecord@nih.gov](mailto:nihrecord@nih.gov).

#### Editor:

Carla Garnett • [Carla.Garnett@nih.gov](mailto:Carla.Garnett@nih.gov)

#### Associate Editor:

Dana Talesnik • [Dana.Talesnik@nih.gov](mailto:Dana.Talesnik@nih.gov)

#### Assistant Editor:

Eric Bock • [Eric.Bock@nih.gov](mailto:Eric.Bock@nih.gov)

#### Editorial Intern:

Amber Snyder • [Amber.Snyder@nih.gov](mailto:Amber.Snyder@nih.gov)

Subscribe via email:

<https://go.usa.gov/x6mgQ>

Follow:

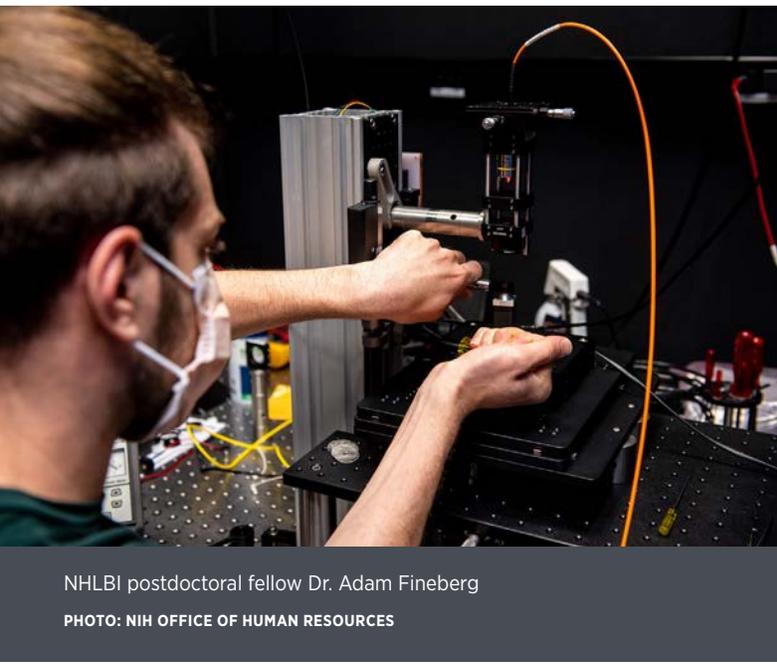
[nihrecord.nih.gov/](https://nihrecord.nih.gov/)



The *NIH Record* is recyclable as mixed paper.



National Institutes of Health  
Turning Discovery Into Health



NHLBI postdoctoral fellow Dr. Adam Fineberg

PHOTO: NIH OFFICE OF HUMAN RESOURCES

## Pivot

CONTINUED FROM PAGE 1

something that's about 100,000 times less than the width of a human hair," Neuman said, describing the individual molecules they're stalking. "That's what we're trying to measure directly. So, this is a very precise, very stable kind of work. And it's all done in real time. This is what's really beautiful. We

watch a single piece of DNA."

The scientists use instruments they build themselves by combining micro-tweezers, video cameras, desktop computers and the software that operates it all. They attach a small magnet to the DNA molecule and then watch as the protein changes the structure of the DNA.

"We see even small, minor moves—up and down," Neuman said.

"We measure and can respond to that in real time. We can see by eye a single enzyme working. And there's something incredibly compelling about that."

When Covid struck in early 2020, the team recently had witnessed significant milestones. They'd seen how solo topoisomerases relaxing overwound DNA might behave when faced with a virtual stop sign—a

chemotherapeutic drug. Neuman pitched an idea to his team: Could they adapt their observations to potential Covid drugs that work by inhibiting viral replication?

"If we had a really good sense of the molecular basis of inhibition—why does this drug work and the next one not work?—then we could get a handle on what's effective, and that may help in producing new drugs," he mused.

The lab's staff scientist and "technical wizard," Dr. Yeonee Seol, immediately seized on the idea.

"As a scientist, particularly as a basic scientist, it's not often you feel like you're contributing in a direct way," Neuman said. "I think she was really upset by what was going on and thought this would be our way to fight back."

About the same time, NIH announced an Intramural Research Program funding competition: Who could pivot to a pandemic-related project? Neuman and Seol wrote up a proposal that became 1 of about 40 to get the green light.

"It's a new view of looking at biology," Neuman said. "This technique we've developed is highly applicable to this situation and has the potential to give us unique insights into how this process of viral RNA replication takes place."

Consider watching 100,000 people gathered in a room, Neuman suggested. Now try to document how each one is behaving.

"You get an average," he said, "but you don't know the details—what [individual] people are doing or what they're thinking. With most work on Covid, replication is done in a test tube"—hundreds of thousands of folks to watch at once. "Think of the single-molecule approach. What we realized from more than a decade of this work is that you learn an enormous amount by understanding what an individual molecule is doing."

Topoisomerases turn out to be an important target for chemotherapeutic anti-cancer drugs. Neuman's group discovered that by observing exactly how individual enzymes are inhibited, he and colleagues can get a deep appreciation for therapy development.

"We thought that by studying the replication process of Covid-19—the so-called RNA-dependent RNA polymerase, how it's inhibited and the molecular details of how this inhibition takes place, which could be



A pre-pandemic view of Neuman's custom-designed lab, specially calibrated for light, sound and motion: The room has two magnetic tweezers. At left, the instrumentation on the table is a magnetic tweezers that also incorporates fluorescence. The full instrument includes the electronics above the table on the rack and one of the computer monitors. The table on the right has a second magnetic tweezers on it. This one is a little more simple but all of the electronics on the right side of the room are part of the instrument, which is controlled by the second monitor on the table. This was all built by hand by the lab's staff scientist, Dr. Yeonee Seol, who often runs both instruments simultaneously from the dual monitor command center in the middle.

PHOTO COURTESY KEIR NEUMAN



In 2019, lab members included (from l) Haksung Jung (departed), Parth Desai, Joe Chapman, Jon Silvers, Shannon Mckie (departed), Keir Neuman, Harry Takagi, Yeonee Seol, James Ferrare (departed) and Rachel Kim. Inset photos are (from l) Harami-Papp, Fineberg and Gabór Harami.

lost or missed in ensemble or traditional biochemical assays—that we may be able to shed light on this process, and help refine [inhibitor drugs such as Remdesivir]...What we do understand [about enzyme-DNA interaction] is exquisitely complex. And what we've learned from this technique is that it's a way of sort of unpacking that complexity."

With the go-ahead and funding from IRP, the lab was able to recruit Dr. Hajnalka Harami-Papp, a visiting fellow from Hungary with expertise in viral biochemistry who will focus on the replication process.

Currently several lab members are preparing substrates, making proteins and otherwise gearing up to tackle this new target in what Neuman describes as less of a full pivot and more of an expansion of their original work. Next steps involve a cross-institute collaboration.

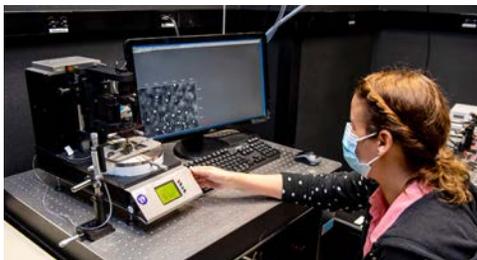
"My colleague Dr. Wei Wang is a structural biologist in NIDDK who also pivoted to some extent to study the structure, not

just of the polymerase, but also as much of that complex as she possibly can," Neuman explained. "And so, our hope is that if she's successful in purifying the whole replication complex—with every single protein involved—then we can leverage her work and study that also at the single-molecule level."

The hardest part of even a partial pivot for groups like Neuman's may be adjusting expectations while confronting a crisis.

"The one trouble with a single-molecule approach is that it's slow and we've all had to learn to be very, very patient," he concluded. "The insights are spectacular, but we measure the activity of a single enzyme. We all know that anecdotes don't carry a lot of weight, right? You can see every detail in this process, but you can't write a paper about one enzyme. We have to collect a hundred or a few hundred individual measurements—and that's per condition. The data collection can be exceedingly slow.

"Some people in the lab get frustrated at times, because we collaborate with people who do more traditional ensemble assays," he continued. "In an afternoon, they can test things that take us weeks to test. And yet, we have this level of detail that is very difficult to achieve with other approaches. So, we get used to things taking a while. And, from what we've all come to understand over the past few years is, [Covid-19] won't be the last [infection] we'll face. There'll always be another one." **B**



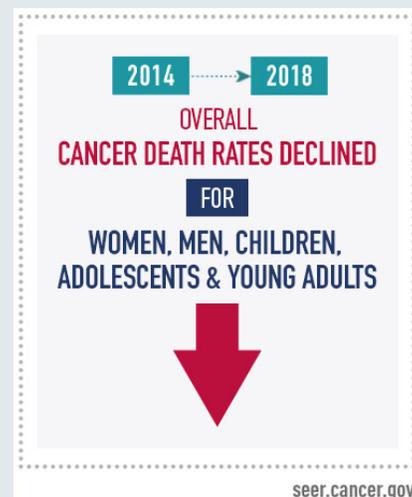
Harami-Papp, a visiting fellow from Hungary with expertise in viral biochemistry, will focus on the replication process.

PHOTO: NIH OFFICE OF HUMAN RESOURCES

## Latest NCI Report Shows Declining Cancer Death Rates

In July 2021, the National Cancer Institute released its annual report to the nation that says overall cancer death rates continue to decline in men and women for all racial and ethnic groups in the U.S. Notably, from 2001 to 2018, lung cancer death rates have declined dramatically and death rates for melanoma declined considerably in more recent years, reflecting a substantial increase in survival for metastatic melanoma.

While death rates declined, the report—a collaborative effort among NCI, CDC, the American Cancer Society and the North American Association of Central Cancer Registries—revealed the overall cancer incidence rates continue to increase among women, young adults and children.



NCI released its annual report to the nation. It says overall cancer death rates continue to decline in men and women for all racial and ethnic groups in the U.S.

The report showed a decrease in death rates for 11 of the 19 most common cancers among men and 14 of the 20 most common cancers among women pre-pandemic, from 2014 to 2018. However, the report also found that for several major cancers, including prostate, colorectal and female breast cancers, previous declining trends in death rates slowed or disappeared. Death rates increased for several cancers including brain and other nervous system and pancreatic cancer in both sexes, oral cavity and pharynx in males, and liver and uterus in females.

For more about the report, see [https://seer.cancer.gov/report\\_to\\_nation/](https://seer.cancer.gov/report_to_nation/).

[HLRCC] that they've said is dangerous. But we've been talking about it for years and it hasn't been dangerous."

When the call came confirming kidney cancer, "I was still on the phone with the doctor," said Jen, "but we could hear Luke in the other room, sobbing. It was such a defining moment in his life, and in ours, and it felt like our world was upside down."

Two days before her son's scheduled surgery to remove his entire right kidney, Jen was searching online and found the HLRCC Family Alliance. Two hours later, an email arrived from its vice chair, Bruce Hatch Lee, Andrew's father.

"I'll never forget receiving that phone call on Dec. 27," said Bruce Lee, president of Driven to Cure, the non-

profit founded by his late son. "We spoke for 90 minutes. I told her, as a patient advocate, if Luke was my son, I'd get a second opinion, especially with the knowledge we now have about not doing radical kidney removals."

Jen took his advice. Two weeks later, she and Luke arrived at NIH.

"Bruce's intervention at that critical time was so powerful, not only because he was connecting us with the world's experts, but also to have someone say, 'I'm going to walk this walk with you; I've been there; I've faced

the worst; I'm here to help you' was just amazing. I didn't realize how much I needed an advocate," Jen said through tears.

### It's His Choice

Even with their cutting-edge imaging technology, NIH's radiology team, led by Dr. Ashkan Malayeri, an expert in HLRCC imaging, could not confirm Luke's mass was malignant. Still, the entire clinical team recommended surgery.

"The amazing thing about NIH's clinical team is that they work together until they have consensus," said Lee. "It's a great, balanced approach and, at the end of the day, the outcome is better."

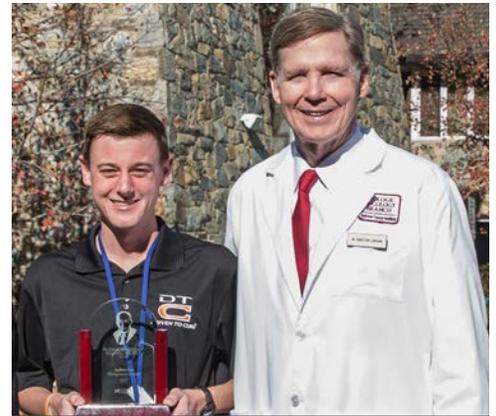
NIH doctors told Luke the surgery

would entail removing only a portion of his kidney.

"We have developed a precision surgery approach over the past 32 years and over 500 HLRCC

patients," explained Dr. Marston Linehan, chief of NIH's Urologic Oncology Branch. "[We don't] do active surveillance with HLRCC tumors—because they can spread from their smallest one-half centimeter—but recommend surgery when the tumor is detected. We do open surgery and we go wide on our surgical margins, because these tumors can spread and infiltrate throughout the kidney."

With the chance the tumor wasn't malignant, Luke decided against surgery.



In 2017, Andrew Lee joins Dr. Marston Linehan for a photo. Lee passed from his illness in 2019.

PHOTO: DANA TALESNIK

His mother, distraught, called Linehan, who reiterated that it's Luke's choice.

"I talked to Luke several times [while he was debating whether to have surgery]," said Lee. "I told him this is a life-and-death scenario and waiting could affect his future outcome. I told him he was in the best place and, even if they couldn't confirm the cyst was [cancerous], now is the time to get rid of it."

Still unsure, Luke consulted Linehan again. Linehan told him: Wait until you're ready but know this won't get better. You'd be closely monitored and will need surgery at some point.

Luke consented. The next morning, a complex, dangerous-looking mass was removed. The surgeon told him, "We're very glad it's out of you."

### Catching It Early

"For HLRCC, we know the key is to act

★ ★ ★  
*"It can be taxing logistically to screen every year... But the tradeoff is, if something does come up and we catch it early, it could be a curable event."*

—DR. MARK BALL

★ ★ ★



Luke Schmaedeke (l) gets wheeled into surgery at NIH. At center, Luke and his mom Jen pose next to the Driven to Cure Nissan GT-R. The car originally belonged to Andrew Lee, and is still used as a fundraising vehicle. At right, Luke takes his mom for a spin around campus in the GT-R, painted orange for kidney cancer awareness.



The Schmaedeke children with their parents, in December 2020: (from l) Corrine (22), Luke (20), Mark and Jen, Isaac (24) and Luke's twin Allison

early, when [cysts] are small,” said Luke’s NIH surgeon, Dr. Mark Ball, who performed a partial nephrectomy, sparing about 85 percent of the kidney.

Through experimental imaging, said Ball, a photon-counting CT “showed a lot more detail, where it looked like a solid tumor. That’s what it turned out to be...Thankfully, this was confined and caught early enough.”

Luke also benefited from new guidelines—thanks to advocacy efforts led by Bruce and NCI—that recently lowered the recommended age for HLRCC screening from 21 to 8.

“We’ve seen tumors in children as young as 10 and people as old as 77,” said Linehan. Annual screens are critical because HLRCC presents a lifelong risk.

“This is definitely a knowledge is power situation,” said Ball. He tells HLRCC patients, “It can be taxing logistically to screen every year. It’s also anxiety-provoking. But the tradeoff is, if something does come up and we catch it early, it could be a curable event.”

### Diagnosing HLRCC

People with HLRCC have a pathogenic variant of one copy of the FH (fumarate hydratase) gene.

The Schmaedeke family first learned they had this variant in 2013, a year after Jen’s mother, Connie, participated in a research study for breast cancer at the Mayo Clinic. Connie had checked a box on the consent

form asking to be notified if any health concerns were identified from her whole-genome screen. A Mayo doctor later called to say she had HLRCC, should get annual scans and alert her family to do the same.

“I was in the middle of raising four teenagers,” said Jen, “and did not pursue testing [at that time].”

Jen learned she had HLRCC in 2016, but waited to test her kids, who were all still under 21. Two years ago, Luke’s older sister, Corrine, got tested when she turned 21 and learned she too had HLRCC.



Bruce Lee poses by the tree, on the Clinical Center’s south lawn, planted in his son Andrew’s memory.

PHOTO: DANA TALESNIK

Although only 19 at the time, Luke spontaneously got tested while tagging along with Corrine for her first annual MRI. Luke tested positive. Getting that first MRI 6 months later likely saved his life.

HLRCC is diagnosed through genetic testing, generally done when there’s a family history of kidney cancer. Another way to diagnose it is by recognizing the signature benign nodules called leiomyomas—the L in HLRCC.

An estimated 15 percent of HLRCC patients develop kidney tumors. “By the time Andrew was diagnosed,” recalled Bruce, “he was riddled with cysts and lesions. HLRCC is too often misdiagnosed or missed altogether.”

### Recent Advances

Tireless advocacy by the Lee family has increased awareness of the disease and the importance of screening. Now, more dermatologists and gynecologists are recognizing leiomyomas, leading to earlier diagnoses and monitoring.

Major advances continue in imaging technology and surgical techniques and for treating patients with advanced disease.

“This approach, developed with and confirmed in clinical trials by NCI oncologist Dr. Ramaprasad Srinivasan, is becoming the worldwide standard for frontline therapy for patients with advanced HLRCC kidney cancer that was based on work in NCI laboratories,” said Linehan. And, by studying donated patient tissue, the team recently made additional discoveries they hope will lead to even better therapies.

The Schmaedeke family discovered firsthand that knowledge is power.

“I realize we could’ve waited until Luke was 21 [to screen and find the tumor],” Jen said. Instead, they caught and removed a tiny tumor when Luke was 19 and he recovered quickly. He was back in class 10 days after surgery and returned to pitching for his college baseball team for the spring season.

Jen is also grateful her mother checked that box on her study form that led to her HLRCC diagnosis.

“All these pieces of the puzzle had fit together to lead us to Luke’s very early diagnosis,” she said. “This is a gift. Luke [initially] didn’t see it that way, but, [looking back], we certainly saw this as a chain of events that ended in something miraculous.” <sup>R</sup>



In the grid at left, participants in a “Diversity of the Social Brain” symposium addressed some of the most burning questions in social behavior. In the grid at right, the 2021 BRAIN meeting featured a session on CRISPR and genome editing with keynote speaker Nobel laureate Dr. Jennifer Doudna, NIH director Dr. Francis Collins and BRAIN Initiative director Dr. John Ngai.

## BRAIN

CONTINUED FROM PAGE 1

virtual for the second time in 2 years.

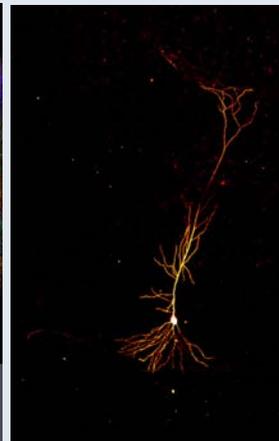
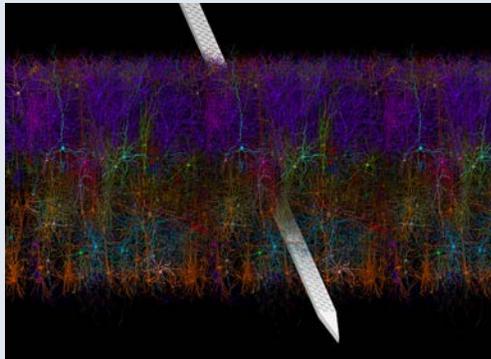
The meeting—which allowed BRAIN researchers to share scientific developments, explore possible new directions and identify areas for potential collaboration—featured keynote plenary sessions, focused symposia, research highlight talks and trainee presentations.

Attendees were able to explore more than 600 scientific posters, showcasing cutting-edge research from hundreds of BRAIN Initiative researchers, and visit a selection of virtual exhibit booths. As a bonus and new this year were video and chatroom options for attendees to engage with poster presenters, exhibitors and speakers as well as opportunities to network with peers.

The 3-day assembly was packed with science talks covering the spectrum of

neuroscience on topics such as Development of Brain Stimulation Responsive to Neural Dynamics, Transformative Potential of the Human Brain Cell Census in Health and Disease, Olfaction: From Sensation to Behavior, and Diversity of the Social Brain.

Each day provided special highlights. Day one included an examination of the ethical implications of CRISPR and genome editing for biomedical research. Moderated by NIH director Dr. Francis Collins, the session



Neuropixels probe was created using a new tool, Visual Neuronal Dynamics.

Third Place: **“Neuron on Fire.”** Olesia Bilash, NYU. Hippocampal CA1 pyramidal neuron in the mouse, recorded from

Photo contest winners (from l), first, second and third places

### Image Contest Winners Announced

Winners of the 2021 Show Us Your BRAINS! Photo and Video Contest—which showcases cool, eye-catching images from BRAIN scientists—were announced June 16.

Winning photos are:

First Place: **“Thinking About a Greener Future.”** Allen Yen, Washington University School of

Medicine. Mouse brain showing green AAV-transduced cells in the cortex and hippocampus. Neurons are labeled red and nuclei are blue.

Second Place: **“Model of Mouse V1 with a Neuropixels Probe.”** Barry Isralewitz, John Stone, Mariano Spivak, Kael Dai, Josh Siegle, Emad Tajkhorshid, Anton Arkhipov, University of Illinois at Urbana-Champaign and Allen Institute. Rendering of a model of mouse primary visual cortex with a

the distal dendrite using patch clamp electrophysiology. The recorded location is visible as the gap in the dendrite. The neuron was filled with biocytin during recording and immunostained with streptavidin-647 post hoc. Confocal image was filtered using ImageJ.

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

featured keynote speaker Nobel laureate Dr. Jennifer Doudna.

“I think CRISPR is a wonderful example of the power of small science and curiosity-driven research to drive new technologies, because this work really came about through the efforts of a small number of laboratories around the world who were investigating a bacterial immune system known as CRISPR, how it worked, and ultimately, that research led to its use and its being harnessed as a technology for genome editing,” said Doudna, professor at the University of California, Berkeley, where she holds the Li Ka Shing chancellor’s chair in biomedical and health sciences.

Day 2 introduced “flash” trainee highlight presentations selected from an abstract competition. During these 4-minute talks and scientific poster presentations, 30 trainee awardees gave overviews of their specific contributions to broader BRAIN Initiative projects. Participating trainees included a variety of scientists from high school, undergraduate and graduate programs, medical and other professional schools, and postdoctoral fellows and residents.

On day 3 several special sessions occurred. One focused on ways to engage the next generation in STEM that featured a panel of young scientists including winners of this year’s BRAIN Neuroethics Essay and Video Challenge. The group shared ideas for reaching out to young people that can be implemented across different areas and career stages.

Jamie Talan, national science writer and clinical assistant professor of science education at Donald and Barbara Zucker School of Medicine at Hofstra/Northwell led a science communication workshop, “My Dream Job: Covering the Brain for 40 Years.” She spoke about how important it is for researchers to have relationships with science writers and

to be able to talk about their work with the media.

“Everybody has a story to tell whether you’re at the back end of something, whether you’re just collaborating, whether you’re doing a clinical trial, whether you’re doing cutting-edge research,” she said. “It’s always a story and you just have to map out what’s important to you in terms of the message.”

The meeting concluded with a dialogue on diversity, equity and inclusion, and



networking opportunities via live video chats. This final plenary panel discussed strategies to build more inclusive networks in the workforce.

“We can do better service by incorporating diverse perspectives whether they are from different disciplines, people from different training and career stages, people from different personal backgrounds as well as people from different institutions and different parts of the world,” said Ngai. “All of this is in service of our goals of democratizing the many resources that BRAIN and others are supporting in this critical space for the benefit of all.”

Since its beginning, the BRAIN Initiative has integrated a focus on neuroethics within its research activities. This year, a special session considered “Perspectives on the complexities of improving neuroethics

engagement among writers, neuroethicists and scientists in academia and industry.”

Dr. Kafui Dzirasa, K. Ranga Rama Krishnan associate professor at Duke University, provided remarks on real-world applications of neuroethics engagement, before attendees broke into small-group discussions. A symposium brought panelists together to discuss achieving diversity, equity, and inclusion in neuroscience research in under-served, under-resourced, and remote settings, and a meeting poster category highlighted neuroethics as a topic.

Posters, exhibit materials, session broadcasts and resources are available free of charge on-demand through June 2022 at <https://www.brainmeeting2021.com/en/#ondemand>.

Launched in 2013, the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative is a large-scale effort funded by NIH, other government agencies and private organizations to revolutionize our understanding of the human brain. **R**

## EDI Schedules Month-Long Virtual Symposium

Join the Office of Equity, Diversity, and Inclusion (EDI) Resolution & Equity Division (R&E) for a month-long virtual symposium, Commit to Progress. Understand your rights and learn how to be an effective ally as we continue to cultivate a workplace that celebrates equity, diversity and inclusion.

### Aug. 9-13 Whistleblowing

- Tuesday, Aug. 10, 11:30 a.m.-1 p.m. Whistleblower 101
- Thursday, Aug. 12, 11:30 a.m.-12:30 p.m. Why Do We Really Hate Whistleblowers? (with Kelly Pope)

### Aug. 16-20 Anti-Retaliation

- Tuesday, Aug. 17, 11:30 a.m.-1 p.m. Anti-Retaliation (for employees)
- Thursday, Aug. 19, 11:30 a.m.-1 p.m. Anti-Retaliation (for managers and supervisors)

### Aug. 23-27 Meet R&E

- Monday, Aug. 23, noon-1 p.m. Meet R&E
- Wednesday, Aug. 25, noon-1 p.m. Meet R&E

Check the EDI blog ([edi.nih.gov/blog](https://edi.nih.gov/blog)) throughout August for insights from the R&E team. Follow the campaign on social media using #NIHCommitToProgress. For details, check [edi.nih.gov](https://edi.nih.gov) and follow us on Twitter, Instagram and LinkedIn.

## Initiative Funds Projects to Safely Return Children to In-Person School

NIH is funding five additional projects to identify ways of safely returning students and staff to in-person school in areas with vulnerable and underserved populations. The awards are the second installment of the Safe Return to School Diagnostic Testing Initiative, part of NIH's Rapid Acceleration of Diagnostics Underserved Populations (RADx-UP) program.



NICHHD is funding projects to identify ways to safely return students and staff to school.

PHOTO: KALI9/GETTY IMAGES

The new awards will fund 5 projects over 2 years in California, Arizona, Hawaii, Nebraska and Florida. The 8 initial awards, totaling \$33 million over 2 years, were made in April 2021.

The program addresses the needs of children with unequal access to Covid testing as well as those facing barriers to attending school remotely, including children who lack access to computers and internet connectivity, or who may not have family members available to help with virtual learning.

Without in-person schooling, many children miss out on school-based meals, speech or occupational therapy and after-school programs. Loss of such services disproportionately affects minorities, the socially and economically disadvantaged and children with various medical complexities.

The new projects will focus on implementing Covid-19 testing regimens for students younger than age 12 (who are ineligible for vaccination), exploring the influence of vaccination for eligible staff and students, addressing vaccine hesitancy and seeking information on circulating variants and breakthrough infections. One of the new projects will focus on native Hawaiians and other Pacific islanders, groups not addressed in the previous awards.

Dr. Diana Bianchi, director of NICHHD, which is managing the initiative, said, "By learning best practices and methods through research, we can get children back in the classroom safely and equitably."

## Developing a New Kind of Temporary Pacemaker

Researchers developed a wirelessly powered temporary pacemaker that breaks down in the body after use. The device can generate enough power to pace a human heart without causing damage or inflammation. The findings appeared in *Nature Biotechnology*.

Pacemakers send electrical pulses to help the heart beat at a normal rate and rhythm, or to help the heart chambers beat in sync. Sometimes people only need a temporary pacemaker, which uses wires connected to a power source outside the body. But temporary pacemakers can cause complications, including infection from the wires crossing the skin, scar tissue formation and damage to the heart upon removal.

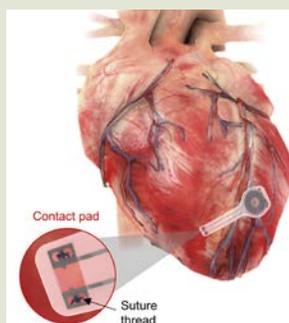
Researchers built a new pacemaker entirely from components that break down in the body over time. The device gets power using technology like that used for wireless charging of portable electronic devices.

"Our wireless, transient pacemakers overcome key disadvantages of traditional temporary devices and eliminate the need for surgical extraction procedures," said lead author Dr. John Rogers of Northwestern University.

The team first tested the new dissolvable pacemaker in heart-tissue samples taken from mice, rabbits and people. In these samples, the device could absorb and transmit enough power to control the rhythm of either the upper or lower chambers of the heart.

When implanted in live dogs, the pacemaker absorbed enough power to control the heart's rhythm. This required the wireless charger to be about 6 inches from the chest or closer. The power generated was equal to that required to pace a human heart.

For longer-term studies, the team implanted smaller versions of the device into rats. The pacemaker was able to control the heart's ventricles for 4 days after surgery. After that, its function began to break down. Using serial CT scans, the team found that the pacemakers broke down entirely in the body by the seventh week after surgery.



A transient pacemaker mounted on the heart

IMAGE: NORTHWESTERN/GWU

Further analysis of the scans showed that heart tissue was unharmed by the device. Blood tests also found no signs of inflammation. Further work will be needed before testing in people.—adapted from *NIH Research Matters*

## Higher-Dose Buprenorphine May Enhance Opioid Use Disorder Treatment Outcomes

High-dose buprenorphine therapy, provided under emergency department (ED) care, is safe and well tolerated in people with opioid use disorder experiencing opioid withdrawal symptoms, according to a NIDA study through the Helping to End Addiction Long-term (HEAL) Initiative.



PHOTO: HAILSHADOW/GETTY

Lower doses of buprenorphine,

an FDA-approved medication to treat opioid use disorder, are the current standard of care. However, elevated doses may provide a critical extended period of withdrawal relief to people after being discharged from the ED that may help them navigate barriers to obtaining medications. The findings appeared in *JAMA Network Open*.

Some EDs already use higher doses of buprenorphine in response to the increasing potency of the illicit opioid drug supply and commonly encountered delays in access to follow-up care, but this practice had not been evaluated.

In this study, researchers analyzed electronic health records documenting 579 ED visits at the Alameda Health System-Highland Hospital in Oakland, Calif., made by 391 adults with opioid use disorder. Many of the patients were from vulnerable populations, with 23 percent experiencing homelessness and 41 percent having a psychiatric disorder.

In 63 percent of cases, the clinicians administered more than the standard upper limit of 12 mg of sublingual buprenorphine during ED induction, and in 23 percent of cases, patients were given 28 mg or more. The higher doses were safe and tolerable. Among those given higher doses, there were no reports of respiratory problems or drowsiness—possible side effects of the medication. The small number of serious adverse events that occurred were determined to be unrelated to high-dose buprenorphine therapy.

Study leader Dr. Andrew Herring of Highland Hospital said that adjusting the dose in the ED "along with resources and counseling aimed at facilitating the transition to outpatient services, may provide the momentum needed to access continuing care."

## Alter Retires After 21 Years at NCI

In June 2021, Dr. Blanche P. Alter, senior clinician in the NCI Clinical Genetics Branch, retired after 21 years of service. Alter is an internationally renowned scholar of cancer-prone genetic syndromes, particularly hematologic bone marrow failure disorders.

In her tenure at NCI, Alter developed and led the inherited bone marrow failure syndromes (IBMFS) study, an interdisciplinary clinical research program to conduct systematic investigations of cancer in families with IBMFS, including Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, and Shwachman-Diamond Syndrome and others. With this study, she led her team to champion novel diagnostic methods, find new causative genes and help families manage serious illness.

During a career spanning 5 decades, Alter was prolific in publishing more than 350 peer-reviewed articles, books and book chapters. She has received many awards for her groundbreaking research, including the NIH Merit Award for her integral role in the IBMFS Study (2009), the Gluckman Lifetime Achievement Award (2014), NIAID Merit Award (2014) and was nominated a Luminary Speaker in 2019 by the American Society of Pediatric Hematology/Oncology.

In addition to her roles as researcher and clinician, she has also been an excellent mentor who provided guidance and encouragement to many young scientists. More than 20 fellows and interns have benefited from her generous mentorship and have gone on to fulfilling careers in medicine, epidemiology and other scientific disciplines.

Before coming to NCI, Alter was chief of pediatric hematology/oncology at the University of Texas Medical Branch (UTMB) and held professorships in pediatrics at UTMB, Mount Sinai School of Medicine and Harvard Medical School. She received an M.D., completed an internship and residency in pediatrics and obtained an M.P.H. from Johns Hopkins University School of Medicine.



Dr. Blanche P. Alter

Alter is board certified in pediatrics and in pediatric hematology/oncology, and is a fellow of the American Academy of Pediatrics and an elected member of the Association of American Physicians. She has sat on dozens of boards and committees and has served as a reviewer for many top-tier journals, including *Annals of Medicine*, *Cancer Epidemiology*,

*Biomarkers & Prevention* and *New England Journal of Medicine*.

Alter's unique and comprehensive IBMFS cohort study will continue to advance understanding of the underlying biology of these syndromes, their connection with cancer etiology and their clinical manifestations.

Following retirement, she will serve as a special volunteer to NCI's Division of Cancer Epidemiology and Genetics.



Dr. Leonard Henry "Pug" Evans

## Mouse Retrovirus Expert Evans of RML Dies

Dr. Leonard Henry "Pug" Evans, 77, chief of the retroviral molecular biology section at NIAID's Rocky Mountain Laboratories in

Hamilton, Mont., unexpectedly passed away in the early morning of June 24.

After earning a Ph.D. from Oregon Health Sciences University, Evans was recruited to the Laboratory of Persistent Viral Diseases by Dr. Bruce Chesebro in 1980. Evans studied murine leukemia viruses at OHSU under Dr. David Kabat and continued studying retroviruses as a postdoctoral fellow under Drs. Peter Duesberg and Edward Scolnick at the University of California at Berkeley.

Evans was the "go-to" guy for information on mouse retroviruses and was an extremely careful and thorough scientist. His key discoveries included finding a glycosylated form of a retroviral gag protein encoded by exogenous, but not endogenous, retroviruses that protected them from host-mediated hypermutation by APOBEC3. He also showed that infections with exogenous viruses could mobilize the production of endogenous retroviral virions, which in turn could influence immune responses.

At the onset of the SARS-CoV-2 pandemic, Evans devoted his full attention to developing a therapeutic for Covid-19—studies that will now miss his leadership role. He was a beloved research mentor, and outside the lab he was known for his cooking skills and hosting the best parties in the Bitterroot Valley.

He is survived by his wife, Janice Dalton-Evans, and daughter, Julia (Stacy) Lockhart. He was preceded in death by his first wife, Patricia. **R**

## VOLUNTEERS

### Gene Therapy Study Recruits

NHLBI researchers, in partnership with Loyola University Chicago, seek individuals with kidney cancer for a new treatment study using gene therapy. Gene therapy is a process of modifying a person's immune system to create tumor-fighting cells to recognize and kill cancer. Study-related procedures, tests and medications are provided at no cost. For more information, call the Clinical Center Office of Patient Recruitment 866-444-2214 (800-877-8339 TTY/ASCII). Self referrals welcome. <https://go.usa.gov/xVhXH>. NIH study 18-H-0012.



**'Christmas in July' Returns to Children's Inn**

On July 21, the Children's Inn at NIH once again welcomed Santa and his merry elves—many on motorcycles—for the 6th annual Christmas in July experience.

The event, made possible by the Montgomery County Police Department with help from the NIH Police, brings gifts, stockings, as well as the joy, comfort and spirit of the holiday season to children participating in research at NIH and their families.

Santa arrived amid much fanfare in a pickup truck via police-led motorcade, bearing dozens of festively wrapped goodies.

