

FROM AMPUTEE TO ADVOCATE Rwandan Trainee Takes Steps to Help Others

BY DANA TALESNIK

There was a time when Claudine Humure was not sure she would ever walk again or even survive. Now, she's climbing to new heights and aspiring to help others in her home country.

A master's student in prosthetics and orthotics at the University of Washington, Humure plans to return to her native Rwanda after training to improve prosthetic care for those who have lost limbs. Her professional journey is a deeply personal one. She shared her story at a Sept. 7 Fogarty International Center-National Institute

of Child Health and Human Development co-sponsored lecture.

At age 6, Humure lost both of her parents in the aftermath of the Rwandan genocide.

She and her siblings were raised in an orphanage, where fortunately she found solace and kindness. But at age 12, her health began declining and it took many months to get a diagnosis.

It was incredibly difficult "sitting in the unknown for so long with constant, chronic pain that did not seem to be relieved by any sort of pain medication," she recounted. "I had lost all hope of ever recovering because, by that time, I had been in front of so many doctors who failed to diagnose my illness."

In 2005, she became one of the first patients of the late Dr. Paul Farmer, whose nonprofit Partners in Health [PIH] had just expanded its health care operation into Rwanda.



"I have come a long way since my first prosthesis. It's this kind of milestone that keeps me driven and believing that Rwandan amputees can also have the opportunity to work and climb mountains again," says Claudine Humure.

SEE **PROSTHETIC**, PAGE 4



FAES scholar house ribbon cut. See story, p. 12.

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Sen. Roy Blunt (R-MO) speaks at CARD facility dedication on Sept. 19.

NIH Dedicates Alzheimer's Research Facility to Blunt

BY ERIC BOCK

NIH recently dedicated its new intramural Center for Alzheimer's and Related Dementias (CARD) research facility to Sen. Roy Blunt (R-MO), a longtime champion of public health research funding.

Many key leaders came together to honor Blunt at the dedication ceremony on Sept.

Miniature Models Made to Aid Drug Development

BY AMBER SNYDER

Tissue built by a 3-D bioprinter. Miniature organs grown on petri dishes or cells grown on "chips."

Aside from sounding like medical technology from the future, these innovations all share something else: they are all microphysiological systems. And many of them are already in use at NIH.

"The naming can be confusing," said Dr. Marc Ferrer, director of the 3-D Tissue Bioprinting

Laboratory at the National Center for Advancing Translational Sciences. "Some



Dr. Marc Ferrer

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SEE **INNOVATIONS**, PAGE 8



NEI To Host 5K Walk/Run/Roll, Oct. 19

On Wednesday, Oct. 19, the National Eye Institute will host its third 5K "Walk/Run/Roll" event on the NIH campus. The course will begin (rain or shine) on the lawn in front of Bldg. 1.

Starting at 11:45 a.m., NIH Recreation and Welfare Association fitness instructors will lead a warm-up, followed by welcome remarks from NEI director Dr. Michael F. Chiang. Music, exhibitors and a VR simulation of eye diseases are also scheduled.

The race starts at 12:10 p.m. Participants will exit campus and travel the perimeter and return through security. The event is open to all at NIH and to the public.

To register and for more information, visit www.nei.nih.gov/nei5k.



EDI Launches Podcast, *What Women Want...at Work*

A lively and informative podcast has people talking! *What Women Want...at Work*, hosted by Joy Postell, women's employment portfolio strategist in the Office of Equity Diversity and Inclusion (EDI) and chair of the women's engagement committee (WEC), is a new initiative by EDI.

Born out of the qualitative and quantitative data surrounding issues women face, WEC strategizes how to eliminate career growth barriers for women. The dialogue grew so rich with thought-provoking content, WEC shared their conversations with other women and allies.

The debut challenges how we think about issues, validate experiences and effect positive change. The first episode aired on the EDI365 YouTube channel, "Women in IT," was enthusiastically greeted.

Guests included NLM director Dr. Patricia Brennan,

Germain, Vosshall Set for Two WALs, Two Kinds of 'Bugs'

The Wednesday Afternoon Lecture Series will feature two high-profile lectures in October.

First up is Dr. Ron Germain, who will deliver the annual William E. Paul Lecture on Oct. 19 at 2 p.m. ET. This talk honors the legacy of Paul, a leader of the NIH community whose career was without parallel in the field of immunology. He died in 2015.



Dr. Ron Germain

Germain is chief of the NIAID Laboratory of Immune System Biology as well as its lymphocyte biology section. He will speak about "Gaining New Insights into 'Fundamental Immunology' Using Imaging and Computation."

An internationally recognized immunologist and member of both the National Academy of Sciences and of Medicine, Germain is known for his innovative in-vivo imaging, analysis and modeling of immune cell dynamics.

On Oct. 26, Dr. Leslie Vosshall will deliver an NIH Director's Lecture titled "Bitten: Why Are Some People More Attractive to Mosquitoes Than Others?"

Vosshall, the Robin Chemers Neustein professor and head of the Laboratory of Neurogenetics and Behavior at Rockefeller University, became HHMI vice president and chief scientific officer in 2022.

She seeks to understand how environmental cues and internal physiology work together to guide complex animal behaviors. She and her team study

this problem in mosquitoes and humans, applying approaches in neurobiology, behavior, genetics and genomics. She uses CRISPR/Cas9 genome-editing tools to advance understanding of how the mosquitoes that spread dengue and yellow fever integrate sensory cues to hunt their human hosts.

Both lectures will be held in Lipsett Amphitheater, Bldg. 10, and viewable online live via NIH videocast.

To attend in person, contact WALSoffice@od.nih.gov so that the number of attendees can be monitored for Covid-19 safety reasons.

More information about WALs is posted at <https://oir.nih.gov/wals>.



Dr. Leslie Vosshall

and CIT communications director Sarah Moffat. Viewership responses ranged from "I never realized there was a connection between information technology careers and health research" to "the guests were so encouraging and knowledgeable."

The second episode illuminated challenges like workplace microaggressions. Postell facilitates a discussion on this sensitive topic by offering tools to respond effectively to microaggressions and become an advocate for safe spaces.

Participants included Rosalina Bray, extramural staff training officer, Clinical Electives Program; Dr. Erika Barr, director, Community College Programs & Summer Opportunities to Advance Research, Office of Intramural Training & Education; Kiana Atkins, principal strategist, Black employment portfolio, EDI; and Olive Jung, predoctoral postbaccalaureate Intramural Research Training Award fellow at NCATS and MD-DPhil candidate in the NIH Oxford-Cambridge Scholars Program.

Podcast episodes can be found on EDI's YouTube's podcast playlist at <https://bit.ly/3SCnXfY>.

NLM Reading Room Reopens

The National Library of Medicine resumed Reading Room operations on Oct. 3. Due to renovations underway in the NLM building, as well as ongoing Covid-19 considerations, services have several changes from those provided prior to the pandemic.

NLM welcomes users by appointment only Monday through Friday from 8:30 a.m. to 5 p.m. ET. To make an appointment, call 1-888-346-3656 Monday through Friday 9 a.m.-5 p.m. ET.

Users will work temporarily in room B1E08, the Billings Conf. Rm. The Reading Room can accommodate up to four users at a time.

Find more information on using the Reading Room on the NLM website: <https://www.nlm.nih.gov/readingroom/index.html>.

NIAMS Trainees Gain Professional Development Skills at Retreat

BY STEPHANIE MATHEWS

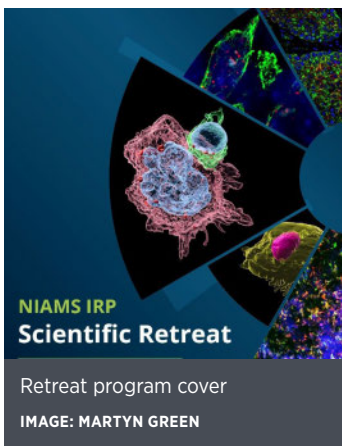
Each summer, labs across the NIH welcome college students and recent grads eager to jumpstart their biomedical research careers. The junior scientists dive into lab work and conduct innovative experiments designed to fill knowledge gaps in their chosen area of study. For NIAMS trainees, the institute's annual IRP Scientific Retreat offers important professional development opportunities.

The retreat brings together NIAMS investigators, trainees and staff to discuss research and clinical advances in diseases of the bones, joints, muscle and skin. This year speakers also touched on

topics such as cancer, inflammatory responses to disease states and public health efforts.

The 2-day event can invigorate senior scientists but it can be intimidating for trainees in the early

stages of their research careers, when they are still learning how to formulate research questions



NIAMS trainees Karyssa Stonick (l) and Danielle Reed

and manage projects. Yet, the retreat offers junior scientists a chance to learn about interdisciplinary approaches and get exposure to diverse fields of study. Casting a wide net helps spark creativity and might help trainees identify new approaches to apply to their own research.

"I enjoyed being exposed to a wide variety of cutting-edge research in rheumatology and related fields," noted Karyssa Stonick, NIAMS summer trainee from Portland State University in Portland, Ore. "The environment allowed my curiosity to flourish."

Trainees also learned effective communication skills by observing oral presentations from intramural researchers and keynote speakers who are experts in their respective fields. Each talk showcased how investigators in different disciplines creatively explain difficult concepts and ask questions to gather knowledge and clarify ideas.

"I witnessed numerous examples of quality science communication, which is invaluable to my growth

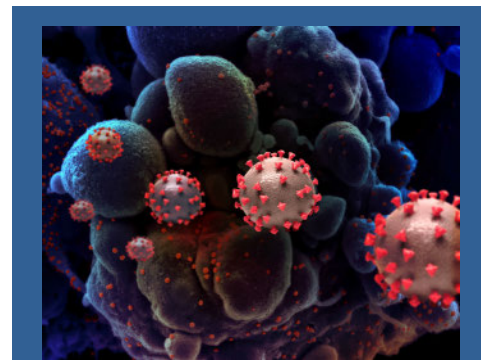
as a scientist," said Danielle Reed, NIAMS postbac trainee from Amherst College in Amherst, Mass.

Trainees also engaged senior scientists in informal discussions, which can open doors to research collaboration.

"I really enjoyed being able to join the poster session breakout rooms and interact with the researchers on a more individual basis," said Stonick. "I was able to practice networking and make new connections."

The retreat concluded with an awards ceremony recognizing trainees who asked the best questions and delivered exceptional poster presentations.

NIAMS trainees left the meeting with an enhanced set of professional skills to carry with them as they embark on their respective scientific journeys. **R**



ON THE COVER: Creative rendition of SARS-CoV-2 virus particles.

IMAGE: NIAID

Registration Now Open for Gender and Health Scientific Workshop Oct. 26

The NIH Office of Research on Women's Health will host a scientific workshop on Gender and Health on Oct. 26.

The virtual workshop titled "Gender and Health: Impacts of Structural Sexism, Gender Norms, Relational Power Dynamics, and Gender Inequities" is being offered in partnership with NICHD, NIA, NIAID, NCI, NHLBI, NINDS, NIMH, NIDA, and OBSSR.



This workshop will convene the extramural community, NIH scientific and program staff and other interested groups and individuals to discuss methods and best practices in biomedical and sociobehavioral research on gender roles, gender norms, gender inequity, and structural sexism.

To view the agenda and register, visit: <https://genderandhealth.vfairs.com/>.

Common Fund Launches 'ComPASS'

The NIH Common Fund recently launched the Community Partnerships to Advance Science for Society (ComPASS) Program to accelerate the science of health disparities and advance health equity research.

The program just issued a research opportunity for community organizations to develop, implement, assess and disseminate community-led, health equity structural interventions. For this opportunity, a letter of intent is required and must be submitted by Nov. 18.

For details, see <https://commonfund.nih.gov/sites/default/files/OTA-22-007.pdf>.



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Turning Discovery Into Health

Prosthetic

CONTINUED FROM PAGE 1

At first, they incorrectly treated her for tuberculosis of the knee only to realize the medication wasn't helping. Farmer then took a biopsy and sent it to colleagues at Massachusetts General Hospital in Boston, where Humure received her diagnosis.

"I was still recovering from my second surgery when I was finally diagnosed with osteosarcoma—bone cancer," Humure said. The recommendation was amputation.

"The cancer had already eaten all of my proximal tibia and was making its way down the whole bone into my fibula," said Humure. Having her leg amputated "was the most traumatic and worst experience of my life thus far...but I am now grateful to still be alive."

The PIH team arranged for Humure to travel to Boston to get chemotherapy and additional surgery. At Mass General, she

★ ★ ★

"I am a living example that people with amputation are more than capable of achieving great things."

-CLAUDINE HUMURE

★ ★ ★

was introduced to the world of prosthetics and would take her first step on her first prosthetic leg.

"That first step was monumental for me," she said. "It really felt like a privilege because I had grown up seeing many people with amputation in wheelchairs, or on the streets of Rwanda as beggars, and I constantly imagined my life being the same."

At the time, she didn't speak English, making the experience especially scary.

"Most people living with an acquired limb loss go through months or years of therapy to be able to accept and process their new reality," she said. "For me, that first prosthesis was my therapist. My hope was restored."

After physical therapy, Humure returned to Rwanda to go back to school. A year later, her prosthetic leg broke.

"That's when I noticed the lack of resources around the country, as I traveled from hospital to hospital, looking for a prosthetic clinician who could put my leg



Humure with PIH founder Dr. Paul Farmer, who died in February. "I have been very privileged to see him in the perspective of a patient and then side by side as a colleague and a friend."

back together," she recalled. "Unfortunately, I didn't find one."

This led Humure back to Boston for a new prosthetic leg and to continue her studies.

"There began my journey with advanced prosthetic technology that used microprocessor knees and shock-absorbing feet," she said. "I was able to see how innovations in prosthetic design can be tools that

truly change the future."

With access to the latest technology, she began interning in prosthetic labs.

"I worked on my first transtibial prosthetic socket," Humure said, describing a summer internship at Next Step Bionics and Prosthetics in Newton, Mass. She later interned in the biomechanics group at MIT's Media Lab and at Autodesk, where she learned more about computer-assisted technology.

In 2017, Humure won a \$10,000 genius award from digital publisher OZY Media for designing a low-cost, 3D-printed, adjustable prosthetic socket. She was inspired by conditions in her home country.

Rwandan genocide left behind many amputees; traffic accidents have produced even more. Disability limited opportunities for those who have lost limbs; many are homeless. The need is great for reliable, affordable prosthetics.

One of the most densely populated countries in Africa, Rwanda has experienced unity and growth in the last two decades.

"Unfortunately, despite the wonderful improvements in the health sector, Rwanda's amputee population and the disability community in general remain at the bottom," said Humure. "In fact, in Rwanda and in most low- and middle-income countries, amputation is often in my opinion considered a health care concern as it happens. But once the patient has healed from all the injuries or wounds, they are sent home and almost forgotten."

There are prosthetic clinics in Rwanda, scattered near the capital, but they are understaffed with few resources. Humure





Humure in Rwanda

wants to change that by opening her own prosthetics center, a state-of-the-art facility with clinical care, clinical research and continuing training for staff. PIH—which has opened three hospitals and a university in Rwanda—is her model and inspiration.

“Partners in Health gave me a second chance at life,” she said, and now she wants to return the favor. “I watched firsthand how powerful the PIH model of serving those most in need—by bringing health care and education resources directly to them—can be.”

After graduating from college, Humure returned to Rwanda to work at PIH’s University of Global Health Equity. Now back in the States, she expects to finish her master’s to become a certified prosthetist and orthotist in June 2023, after which she will enter a 2-year residency. Then she plans to focus on making her envisioned prosthetic center in Rwanda a reality.

“I am a living example that people with amputation are more than capable of achieving great things—we are creative and motivated,” she said. “And I have no doubt that my future prosthetic center will help restore hope and boost morale for people living with amputation in Rwanda and in sub-Saharan Africa.” [R](#)

Wegrzyn Named First ARPA-H Director

President Joe Biden intends to appoint Dr. Renee Wegrzyn as the first director of the Advanced Research Projects Agency for Health (ARPA-H), the agency newly established to drive biomedical innovation that supports the health of all Americans.

In announcing his selection on Sept. 12—the 60th anniversary of President John F. Kennedy’s Moonshot speech—Biden talked about his vision for another American Moonshot: ending cancer as we know it. ARPA-H figures prominently among other initiatives to reach that goal.

Describing Wegrzyn as a leading biomedical scientist and an entrepreneur in synthetic biology with a decade of experience leading multiple biotech projects at the Defense Advanced Research Projects Agency (DARPA), Biden said, “It’s about how to use all the assets we have—all of them. She’s going to bring the legendary DARPA attitude and culture and boldness and risk-taking to ARPA-H to fill a critical need. Discoveries that save lives, change lives, often start at the lab bench. But then those basic research breakthroughs need to be tested, scaled and brought to the clinic. This may require unusual partnerships that may require support to get over many obstacles that exist. That’s what ARPA-H is designed to do, so the advances can reach all Americans sooner. I predict ARPA-H will emerge as a new and exciting member of America’s biomedical ecosystem.”

Wegrzyn has professional experience working for two of the institutions that inspired the creation of ARPA-H—DARPA and Intelligence Advanced Research Projects Activity (IARPA). She will be responsible for driving the new agency’s nascent research portfolio and associated budget. The budget is expected to support a broad range of programs to take on challenging health problems in pursuit of high-reward solutions to help everyone.

“President Biden could not have chosen a better inaugural director for ARPA-H,” said HHS Secretary Xavier Becerra. “With Dr. Wegrzyn at the helm, ARPA-H is poised to drive health innovation and launch bold and ambitious

research programs. She will lead us in tackling some of the most pressing health challenges of our time.”

ARPA-H was created earlier this year to push the limits of U.S. biomedical and health research and innovation. Public Law 117-103, which was enacted on Mar. 15, authorized establishment of ARPA-H within HHS. Becerra transferred ARPA-H to NIH on Apr. 14.

On May 25, he formally established ARPA-H as an independent entity within NIH to ensure

its ability to operate autonomously and partner across HHS and the wider U.S. government to identify projects that will be transformative and far reaching.

Previously, Wegrzyn served as a vice president of business development at Ginkgo Bioworks and head of Innovation at Concentric by Ginkgo, where she focused on applying synthetic biology to outpace

infectious diseases—including Covid-19—through biomanufacturing, vaccine innovation and biosurveillance of pathogens at scale.

Prior to Ginkgo, Wegrzyn was program manager in the Biological Technologies Office at DARPA, where she leveraged the tools of synthetic biology and gene editing to enhance biosecurity, promote public health and support the domestic bioeconomy. Her DARPA portfolio included the Living Foundries: 1000 Molecules, Safe Genes, Preemptive Expression of Protective Alleles and Response Elements and the Detect it with Gene Editing Technologies programs.

Wegrzyn received the Superior Public Service Medal for her work and contributions at DARPA. Prior to joining DARPA, she led technical teams in private industry in the areas of biosecurity, gene therapies, emerging infectious disease, neuromodulation, synthetic biology, as well as research and development teams commercializing multiplex immunoassays and peptide-based disease diagnostics.

Wegrzyn holds doctorate and bachelor’s degrees in applied biology from the Georgia Institute of Technology. She was a fellow in the Center for Health Security Emerging Leaders in Biosecurity Initiative and completed postdoctoral training as an Alexander von Humboldt fellow in Heidelberg, Germany.



Dr. Renee Wegrzyn



With the Roy Blunt Center for Alzheimer's and Related Dementias Research as backdrop at the event are (from l) NIA director Dr. Richard Hodes; CARD staff scientist Dr. Sara Bandrés Ciga; former NIH director Dr. Francis Collins; Dr. Dawn Beraud, director of NIA's Office of Legislation, Policy and International Activities; acting NIH deputy director for intramural research Dr. Nina Schor; Blunt; Rep. Tom Cole; and Dr. Lawrence Tabak, who is performing the duties of NIH director. At right, Blunt and CARD director Dr. Andrew Singleton walk through the new facility.

PHOTOS: CHIA-CHI CHARLIE CHANG

Blunt

CONTINUED FROM PAGE 1

19, including Rep. Tom Cole (R-OK) and Sen. John Boozman (R-AR).

"I'm so pleased to be associated with NIH," said Blunt during the ceremony. "I'm particularly pleased to be associated with this critically important building for the future of families and the future of aging and the future of people caring about other people."

Six million Americans have Alzheimer's. One American moves into the Alzheimer's category every 65 seconds; 11 million Americans are caregivers.

By 2050, the cost of Alzheimer's in the U.S. alone will be \$1.1 trillion—equal to today's entire Department of Defense budget. By then, Blunt said, 2 people will get the disease every 65 seconds "unless the promising work happening right now produces results."

The first national plan to address Alzheimer's was created in 2012, said Dr. Lawrence Tabak, performing the duties of NIH director. "Today, we reflect on how far we've come thanks to robust and sustained investment from Sen. Blunt and his colleagues in Congress," he said.

NIH-funded research has led to new discoveries about Alzheimer's and related dementias. Finding effective treatments "has never appeared more promising," Tabak said. "Now, we have to leverage the momentum we've gained to continue innovation and discovery to push forward to improve diagnosis, prevention and treatments."

The 24,000 square foot building will house more than 130 scientists and staff. The center will support basic, preclinical and clinical research. It is made up of 65 individual modular units that were assembled at a

factory outside Orlando, Fla., and delivered by truck for assembly in Bethesda.

"Sen. Blunt's support for NIH and Alzheimer's research in particular has

• • •

"The only way we can assemble teams like that is to build centers...where people can be invited from every possible discipline, from every vantage point, with every view possible of these disorders."

-DR. NINA SCHOR

• • •

been instrumental to important progress in making this center possible," said Tabak. "The naming of this facility recognizes him as an extraordinary leader and pays tribute to his unwavering commitment to speed

progress in dementia research and care."

Developing treatments for Alzheimer's will require experts from different scientific backgrounds working together, said Dr. Nina Schor, acting NIH deputy director for intramural research.

"The only way we can assemble teams like that is to build centers like the Roy Blunt Center for Alzheimer's and Related Dementias Research, where people can be invited from every possible discipline, from every vantage point, with every view possible of these disorders," she said.

In 2020, NIA and NINDS established the center "to fight the growing tidal wave of dementia-related disability," recounted



On a tour inside the building are (from l) the Blunts, Tabak and Singleton observing as NIA postbac Pilar Alvarez Jerez (r) explains CARD's use of long read sequencing to look at complex human genetic variation in Alzheimer's disease in record time. Identification of genes associated with disease will help make strides towards personalized medicine.



"I'm so pleased to be associated with NIH," said Blunt during the outdoor ceremony.

CARD and NIA staff scientist Dr. Sara Bandrés Ciga.

"The CARD fills gaps that exist across basic science, translational, clinical and data science portfolios of Alzheimer's and related dementias research," she said. "We are not here to compete with existing programs. We are here to compliment research through open science, training and collaboration."

Since 2015, Blunt has been the senior Republican on the Senate appropriations subcommittee on Labor, Health and Human Services, Education, and related agencies, the congressional committee that oversees NIH's budget. During his tenure, NIH's funding has increased by nearly 50 percent. Research funding for Alzheimer's has grown five-fold over the past 7 years.

Former NIH director Dr. Francis Collins first got to know Blunt on a visit to Washington University in St. Louis's medical campus. There, they saw presentations on the microbiome, cancer and Alzheimer's. Blunt had insightful discussions with the presenters and met with the younger scientists.

"I knew we had a champion, somebody who was able to ask hard questions and

wasn't going to be a pushover," said Collins, who is currently President Joe Biden's acting science advisor. "He immersed himself in the details right away."

NIH's budget doubled from 1998 to 2003, thanks to the efforts of Congress. Over the next dozen years, "NIH lost ground." The purchasing power for medical research declined by more than 20 percent.

Legislators who had previously boosted NIH research, such as late Congressman John Porter and former Sens. Arlen Specter and Tom Harkin, were no longer around.



Tabak (l) reflects on investment in science by Blunt and his congressional colleagues.

"New giants," like Blunt and Rep. Cole, arose, Collins said. In 2016, NIH started down a path of steady, predictable growth.

"Sen. Blunt has the kind of character we need more of in our world—intelligence, curiosity, integrity, dedication, compassion and selflessness," said Collins.

Blunt has worked closely with Cole,

ranking member of the House subcommittee on appropriations that oversees the NIH budget, to reinvest in biomedical research.

"We saw there had been 12 flat years and we were cognizant of what that meant in terms of the signals we were sending out to young researchers and our position in the



A specially decorated cake made the occasion sweeter for the Blunts and guests.

world," said Cole. In the 7 years since, "NIH has gotten a substantial increase."

When they first talked about increasing NIH's budget, Cole asked Blunt if they should again double the budget like Porter had. Blunt replied, "no," because "once you get to a goal, my experience is you quit doing the thing that got you there."

Instead, Blunt opted for a different target: "inflation plus increase for NIH." Every year, they worked with their colleagues across the aisle, Sen. Patty Murray (D-WA) and Rep. Rosa DeLauro (D-CT), to get it done.

"It didn't matter who was president or which party controlled the House or Senate. The bill got across the line," Cole said. "The most steadfast person in that has been Roy Blunt, who set the goals and standards."

Cole lost his father to Alzheimer's. Although the disease is personal for him, securing funding for Alzheimer's research was a logical decision. Alzheimer's is the most expensive disease. Trying to cure, manage or delay it is cheaper than dealing with it.

"The guy who spotted and focused on that is my friend and leader, Roy Blunt," he concluded. "It's been a wonderful journey and a great honor to be his partner, friend and follower in an endeavor this important."

Closing the event, NIA director Dr. Richard Hodes said his institute is determined to find treatments that delay onset, slow disease progression or treat Alzheimer's. NIA will continue "the tradition of intensity, commitment, inclusiveness and diversity, to the research that is needed to carry us to the finishing line." **R**

Innovations

CONTINUED FROM PAGE 1

people call these complex tissue models organoids, some people call them tissue chips.” But “microphysiological system” encompasses the whole spectrum of these miniature models.

According to the FDA, microphysiological systems (or MPS) are “organoid cell formations of human or animal origin in a micro-environment that provide and support biochemical/electrical/mechanical responses to model a set of specific properties that define organ or tissue function.” MPSs are miniature tissue and organ models grown in the lab with various kind of cells from human tissues. Researchers at NCATS and elsewhere are hoping to use these technologies to solve a major problem in drug development.

“Only about 10 percent of drugs being developed [receive full FDA approval],” said Dr. Danilo Tagle, director of NCATS’s Office of Special Initiatives. “That’s...a 90 percent attrition rate.”

The high failure rate is largely due to the models researchers use to test the drugs, he revealed. 2-D cell culture systems and animal models are typically used to evaluate therapeutics, but they are not very good at predicting a drug response in a human body.

Researchers at NCATS and elsewhere are hoping MPS tech can solve this predictability gap, a big translational problem.



Dr. Danilo Tagle

Toward Better Models

Very often, the effect of drugs in animals cannot be extrapolated into humans because of species differences. 2-D cell culture systems also are inadequate because they involve testing drugs on a single cell type grown as a

monolayer on plastic surfaces—a far cry from being in a tissue- or organ-like environment, with its many different cell types that influence drug responses in a real human. Up until recently, though, these were the best options researchers had.

“We needed a better predictive model,” Tagle realized.

Enter MPSs.

Founded in 2011, NCATS began developing tissue chip technology in 2014. The 3-D bioprinting lab followed in 2018. Organoids and spheroids—the other types of MPSs—pre-date NCATS, but are also being studied by the center.

Making an MPS begins with human cells. Researchers have learned how to convince primary cells—those harvested directly from living tissue or organs—to grow and differentiate into models in the lab.

“We use primary cells when we can,” said Ferrer, noting that they are useful in tissue models like skin, where cells are relatively easy to get. In

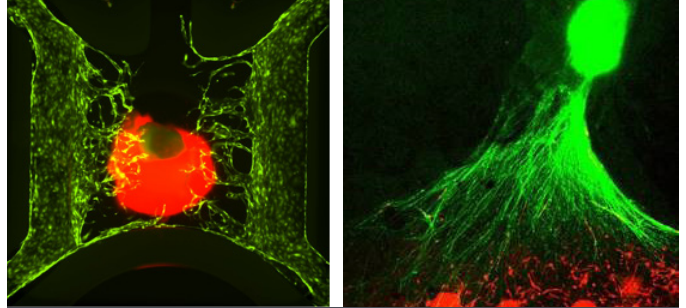
situations where primary cells are not easily obtained, such as the brain, researchers use adult stem cells called induced pluripotent stem cells, or iPSCs.

iPSC cells are typically derived from skin or blood samples and researchers have established guidelines for inducing these cells to become stem cell-like. Like embryonic stem cells, iPSCs are generic cells that can differentiate into any cell type, but iPSCs have the benefit of being sourced from adult tissue.

Spheroids are typically made starting from primary cells, or from iPSC cells that have already been differentiated. Organoids, on the other hand, often start as undifferentiated iPSCs that are then instructed to develop into a certain cell type, said Ferrer.

Challenge—Mimicking Organ Function

Both spheroids and organoids are 3-dimensional clusters of cells; the difference comes from how the cells organize and function within the cluster.



The Robey (NIDCR) and Ferrer (NCATS) labs are using a tissue chip plate to generate a vascularized bone tissue model. At left, a bone organoid (red) in a vasculature (green) tissue-chip

IMAGE: BYRON MUI, MIN JAE SONG, PAM ROBEY, MARC FERRER

The Ward (NINDS) and Ferrer (NCATS) labs are using the bioprinting approach to biofabricate a tissue model of the neuromuscular junction. At right, a motor neuron spheroid forming extensions towards a bioprinted muscle tissue (red).

IMAGE: CRISTINA ANTICH ACEDO, SHAYNE FREBERT, JENNIFER COLON MERCADO, MIN JAE SONG, MICHAEL WARD, MARC FERRER

When scientists make an organoid, they bathe the iPSCs in a fluid containing a mixture of growth factors and other compounds that encourage the cells to differentiate into the desired cell types. These cells then “self-organize” into a cellular-level model of an organ, a process that might take many weeks and even months.

Spheroids, because they are made from mature primary cells, can assemble without differentiating. They’re a “faster way to create 3-D organotypic models,” Ferrer said. Spheroids are less complex than organoids, but are still useful because they have multiple cell types functioning together. Both spheroids and organoids are useful for large-scale drug testing, particularly spheroids because they are easier to make.

Both spheroids and organoids can be used to test drug efficacy, but both also have drawbacks. There is no way to mimic the blood flow that those cells would be exposed to in a real organ, for example. And, because cells in organoids differentiate and self-assemble, it is sometimes difficult for scientists to include all the cell types needed and at the right proportions to mimic an organ.

That is where tissue chips come in. Approximately the size of a USB drive for a single organ system, these technologies are designed to mimic the structure and function of a human organ.

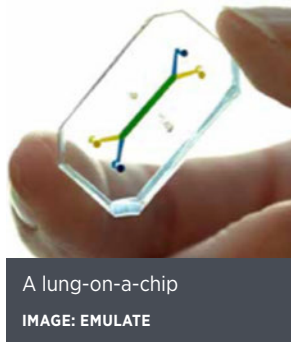
“Organoids and spheroids work well for modeling many tissues and organs, including tumors, colon, liver and brain,” Ferrer said, but “tissue chips are ideal when you need to mimic blood flow and reproduce ‘cross-talk’ between organs.” Researchers can even incorporate multiple organ systems onto a single, playing card-sized chip.

Chips are “probably the most complex and



A 5-organ chip (heart, liver, neuron, skeletal muscle, kidney)

IMAGE: HESPEROS



A lung-on-a-chip

IMAGE: EMULATE

sophisticated way of structuring and copying organ function in [the lab],” Tagle agreed.

model is printed layer by layer using primary or iPSC-derived cells mixed with “bio-ink.”

Ferrer said the process looks “a bit like mixing ketchup and mustard.” It is a labor-intensive and technically difficult process compared to making organoids and spheroids, but has the benefit of producing a much more precise model.

Future Uses

So, what lies ahead for MPSs? NCATS investigators say these devices will vastly improve the accuracy of pre-clinical trial drug screening.

Ferrer envisions using a combination of tissue chips, organoids, spheroids and bioprinted tissue models to aid the process of drug discovery and development. Initially, researchers could weed out ineffective drugs by testing them in a multi-well plate, each well containing a spheroid, organoid or bioprinted tissue, and one compound added to each to test its effect.

After the ineffective drugs are removed, the most promising compounds could undergo additional testing in more sophisticated and complicated tissue chip models.

MPSs also have the potential to complement animal research in drug testing.

“Animal models of disease cannot always capture the entire pathology of human disease,” Tagle explained. He cited the Alzheimer’s mouse model, which has been around for several decades but has not yielded any effective treatments.

MPSs, because they use human cells, are producing much more clinically predictive human models. MPSs are complementing animal research in drug testing. We are not yet at a point where MPSs can replace animal research entirely, he said, but “[they] can easily fill in areas where we can refine our use of animals.”

Next Steps

What will make these more practical to use?

Researchers need to account for diversity in human populations when building MPSs, because different groups may respond differently to certain diseases or treatments.

Another limitation is that researchers have not yet managed to build a model that can replicate a fully functioning adult immune system. And, investigators need to produce consistent results—so, every liver tissue chip in a trial will have the same response to the same drug.

“The challenge is getting [MPSs] out of specialized labs and into the hands of people doing basic, translational and clinical research,” said Ferrer.

At NIH, that is already in motion. NCATS is collaborating with several ICs—NEI, NHLBI, NCI, NINDS, NIAID and others—to incorporate MPSs into their research, as well as with other federal entities such as NASA, VA and FDA. Private companies are also working on their own MPSs.

MPSs “are already making a big impact,” Tagle concluded. **R**

Chip Creation

Making a tissue chip begins with a flexible plastic, which is cut into the desired shape. Then, chambers and channels are added—either by etching or laser. The chambers are lined with differentiated iPSCs, and fluids are run through the channels to mimic functions like nutrient or blood flow. Researchers can also add sensors to measure processes such as pH or oxygenation. The sensors can even simulate mechanical stress.

A lung-on-a-chip, for example, will also have an air-liquid interface, where cells are exposed to air—just like they would be in a real lung.

“It captures the real microenvironment of the tissues” that you’re trying to model, Tagle explained.

‘Ketchup and Mustard’

The final category of MPS is 3-D bioprinted tissue.

Bioprinting employs similar techniques to traditional 3-D printing (but uses biological materials including live cells) to create models that mimic natural tissues. Researchers design the architecture of the tissue in a computer program. Then the

Tuncay 1st to Complete NEI International Fellowship

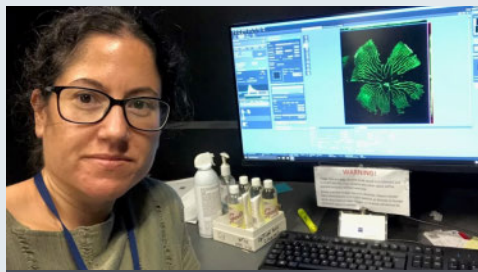
BY KATHRYN DEMOTT

Dr. Fulya Yaylacioğlu Tuncay said she gained crucial experience in translational medicine as the first participant in an ocular genetics fellowship program sponsored by NEI and the International Council of Ophthalmology. She takes home to her native Türkiye hands-on experience, momentum and a new network of collaborators.

“The goal of the NEI-ICO program is to train the next generation of global leaders in vision,” said Dr. Gyan “John” Prakash, director, Office of International Program Activities at NEI. “The fellowship incorporates both clinical and bench research.”

Tuncay, an assistant professor of biology at the University of Health Sciences, Ankara, Türkiye, arrived at NEI in September 2021 for a year-long fellowship in the NEI Ophthalmic Genomics Laboratory.

She analyzed data from NEI’s National Ophthalmic



Dr. Fulya Yaylacioğlu Tuncay learned to prepare slides of zebrafish retina for imaging of blood vessels, a skill she’ll use in her research of inherited retinal diseases in Türkiye.

Disease Genotyping and Phenotyping Network (eyeGENE) to explore the genetic causes of familial exudative vitreoretinopathy (FEVR), a rare inherited disorder of retinal angiogenesis associated with visual loss, especially in the pediatric patients.

FEVR affects vision by preventing blood vessels from forming at the edges of the retina, which reduces the blood supply to the light-sensitive

tissue. She then used a zebrafish model to study the vascular origins of the disease, learning to prepare zebrafish retina for blood vessel imaging.

“Combining benchside and bedside data to inform our understanding of inherited eye diseases in humans was a great experience,” said Tuncay.

In Türkiye, Tuncay plans to continue her work with zebrafish and hopes to identify clinical study cohorts by establishing patient registries. She also has plans for how to share the knowledge she gained at NIH.

“I am excited to see where Dr. Tuncay’s research takes her when she returns home, and I look forward to being her collaborator and colleague,” said Dr. Robert Hufnagel, Tuncay’s mentor and director of the NEI Ophthalmic Genomics Laboratory.

For more on the fellowship, visit <https://icoph.org/ico-fellowship>. No new fellows are being recruited at this time due to the interruption related to the pandemic. NEI hopes to restart the program in the future.

Steroid Treatment May Improve Outcomes in Preterm Infants

Steroid treatment before birth appears to improve survival and reduce complications among extremely preterm infants, according to a recent NIH study funded by NICHD and NCATS. The study appears in *JAMA Network Open*.



PHOTO: PETER BAKO / SHUTTERSTOCK

Antenatal steroid therapy, given to women at risk of preterm delivery, causes the fetal lungs to mature and has been shown to improve survival and reduce complications among infants born from 24 to 34 weeks of pregnancy. However, previous studies of the treatment for infants born between the 22nd and 23rd week—those at greatest risk for death and disability—were inconclusive.

The study was conducted by Dr. Sanjay Chawla at Central Michigan University, Mount Pleasant, and Wayne State University, Detroit, and colleagues at 17 research institutions.

Of the mothers of the 431 infants in the study, 110 did not receive the steroid betamethasone, 80 received partial treatment (1 dose) and 241 received complete treatment (2 doses 24 hours apart).

Of the infants exposed to complete treatment, 53.9 percent survived until hospital discharge, compared to 37.5 percent with partial treatment and 35.5 percent with no treatment. Compared to infants receiving no treatment, infants exposed to full treatment were 1.95 times more likely to survive and 2.74 times more likely to survive without major complications such as severe bleeding in the brain, severe lung disease, cysts in the brain, severe inflammation of the intestines or abnormal blood vessel growth in the retina.

Study authors concluded that their results provide strong evidence to support giving antenatal steroid therapy to pregnant women at risk for delivery at 22 weeks.

Heart Medication Shows Potential for Treating Alcohol Use Disorder

A new NIH study has found that a medication for heart problems and high blood pressure may also be effective for treating alcohol use disorder (AUD).

The study presents converging evidence from experiments in mice and rats, as well as a cohort study in humans, suggesting the medication, spironolactone, may play a role in reducing alcohol drinking. The research was led by scientists at NIDA and NIAAA in conjunction with Yale School of Medicine. A report of the new findings is published in *Molecular Psychiatry*.

“Combining findings across three species and different types of research studies, and then seeing similarities in those data, gives us confidence that we are onto something potentially important scientifically and clinically,” said Dr. Lorenzo Leggio, chief of the clinical psychoneuroendocrinology and neuropsychopharmacology section, a joint laboratory of NIDA and NIAAA.

Currently there are three medications approved for AUD in the U.S. and they are effective treatments. Given the diverse biological processes that contribute to AUD, new medications are needed to provide a broader spectrum of treatment options.

Previous research has shown that mineralocorticoid receptors, located throughout the brain and other organs and that help regulate fluid and electrolyte balance in the body, might play a role in alcohol use and craving. Preclinical research suggests that higher mineralocorticoid receptor signaling contributes to increased alcohol consumption.

The current study sought to expand this line of research. In experiments conducted in mouse and rat models of excessive alcohol drinking, NIAAA and NIDA researchers found that increasing doses of spironolactone decreased alcohol consumption in male and female animals, without causing movement or coordination problems and without affecting their food or water intake.

In a parallel study that was part of this team’s collaboration, researchers examined health records of a large sample of people from the U.S. Veterans Affairs health care system to assess potential changes in alcohol drinking after spironolactone was prescribed for its current clinical indications. They found a significant association between spironolactone treatment and reduction in self-reported alcohol consumption, as measured by a screening tool.

Of note, the largest effects were observed among those who reported hazardous, heavy episodic alcohol consumption before starting spironolactone treatment.

NIDA director Dr. Nora Volkow said, “Just like for any other medical condition, people with substance use disorders deserve to have a range of treatment options available to them, and this study is an exciting step in our effort to expand medications for people with alcohol use disorder.”

Two Diabetes Drugs Outperformed Others in Clinical Trial

In a large, NIDDK-funded clinical trial comparing commonly used type 2 diabetes medications, researchers found that insulin glargine and liraglutide performed the best of four medications FDA-approved to maintain blood glucose levels in the recommended range.

All four medications evaluated were added to treatment with metformin, the first-line drug to treat type 2 diabetes.

More than 37 million Americans have diabetes; approximately 90 to 95 percent of them have type 2 diabetes. People with diabetes who keep their blood glucose levels in the near-normal range generally have a much lower risk of developing diabetes complications such as nerve, kidney and eye diseases. Most people with type 2 diabetes require more than one medication to control blood sugar levels over time.

While there is general agreement among health care professionals that metformin combined with diet and exercise is the best early approach in diabetes care, there is no consensus on what to do next to best keep high blood glucose in check.

Launched in 2013, the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study, was conducted at 36 U.S. study centers. Results were published in the *New England Journal of Medicine*.

The study enrolled 5,047 people with type 2 diabetes from diverse racial and ethnic groups who were already taking metformin. Participants were randomly placed into 1 of 4 treatment groups. Three groups took metformin plus a medicine that increased insulin levels, sitagliptin, liraglutide or glimepiride. The fourth group took metformin and insulin glargine U-100, a long-acting insulin.

After an average of 4 years of follow-up, the study found that participants taking metformin plus liraglutide or insulin glargine achieved and maintained their target blood levels for the longest time compared to sitagliptin or glimepiride. Treatment effects did not differ based on age, sex, race or ethnicity. However, none of the combinations overwhelmingly outperformed the others.

Dr. Henry Burch, NIDDK’s project scientist for GRADE, said the study “is an integral step toward precision medicine for diabetes care, as these results can now be used in the decision-making process for each individual patient in light of their levels of glucose control, how well the medications are tolerated and the person’s other health considerations.”

NCI's Holliday Retires After 34 Years at NIH

Alesha Holliday, director of NCI's Office of Management Policy and Compliance (OMPC), recently retired after more than three decades at NIH.

She arrived at NIH in 1988, after working in a small office supply store in Bethesda, while attending Montgomery College. "Talking to friends at school, customers and co-workers, I realized that the federal government trains its staff to use computers," Holliday recalled. "I started applying right away. My first interview was at NIH with the NIAID. I was hired as a part-time GS-4 grants clerk" working in the Westwood Bldg.

She moved to Bldg. 1 in 1990 for an administrative technician position in NIH's Office of Extramural Research, where she climbed the ranks of administration and management over the next 20-plus years, working in the NIH Office of the Director, NCI Office of Management and at NHLBI, where she served as the acting deputy executive officer for 2 years.

In early 2013, Holliday returned to NCI as branch chief at OMPC. She served as the office's acting director for about 2 years before being selected for the position permanently.

"I first worked with Alesha in the NCI Office of Management Analysis in 2004-2005," said Laura M. Larson, OMPC deputy director, and chief of its Quality Management/Program Integrity Branch. "I learned so much from her in that short time that I was disappointed when I learned that she was leaving for what turned out to be bigger and better things at NHLBI. She had a phenomenal career at NHLBI. While we sort of kept in touch after she left, it wasn't the same. Fast forward to January 2013, when I heard

she was coming back to NCI. It has been the 10 best years of my career working for and alongside Alesha. She's a fantastic motivational leader. Alesha would write various quotes every Friday on our whiteboard for staff while in the office and then continued

that tradition using gifs in Teams. She is often sought out as a mentor. She's definitely a go-to person. Nothing fazes her, whether it involves having to give a last-minute presentation or stepping in to help out a fellow NCI'er who was having trouble singing *Killing Me Softly* at an NCI Talent show. She leaves behind wonderful memories and big shoes to fill."

Over the course of her 34-year federal career, Holliday has received numerous honors and

accolades, including six NIH Merit Awards and an NCI Director's Award in 2021 for Covid-19 survey analysis.

A proud Trinity College alumna whose mission is a continued commitment to educating women, she has nurtured several proteges informally throughout her career and formally as part of the NCI Career Mentoring Advantage Program from 2015 to 2020.

"Working with Alesha over the past 10+ years has been beyond a remarkable and rewarding experience both professionally and personally," said LaKisha Bolden, NCI senior management analyst. "Her 'people first' management style is one that every employee should experience. She always showed how much she cared about you and not just the work that you did. She would always say in work and life 'remember what's really important.' Alesha will forever be remembered and greatly missed for being a leader of integrity, high emotional intelligence and impeccable character."

Holliday also volunteered in several professional and career-development organizations over the years, serving

as recording secretary for the NIH chapter of Blacks In Government, area director and multiple leadership positions with Gene Toasters/Toastmaster International and as a member of Federally Employed Women and the National Alliance on Mental Illness.

Married with two children and a 10-year-old granddaughter, Holliday has already mapped out several post-NIH activities, including expanding her capacity to serve others.

"I plan on becoming an advocate for disability rights," she said, "continuing my charity work, spending more time with my family, and traveling."

Reflecting on her multi-decade career in federal service and the highs and lows of the past few years in particular, Holliday summed up her experiences with a quote from the late actor Chadwick Boseman, "The struggles along the way are only meant to shape you for your purpose. Press on with pride and press on with purpose." **B**



NCI's Alesha Holliday recently retired.



At a CFC talent show in 2018, Holliday sings.

PHOTO: COURTESY LAURA LARSON

VOLUNTEERS

Volunteers Needed for PKLR Gene Study

NHLBI invites volunteers ages 18-80 of African descent with or without sickle cell trait and people with sickle cell disease to participate in a one-time visit research study. Volunteers will provide blood samples that will be used to look for a link between the PKLR gene and pyruvate kinase protein. The PKLR gene is active in the liver and in the red blood cells and helps to create protein called pyruvate kinase that is essential in normal functioning of the red blood cells. Compensation provided. For more information about study #18-H-0146, call 866-444-2214, email ccopr@nih.gov, or visit <https://go.usa.gov/xP8Hx>.

Study Needs Volunteers with CLL/SLL

NHLBI researchers need volunteers with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) for a vaccine study. Researchers are studying how well the following vaccines work in patients with CLL/SLL malignancies: SHINGRIX and influenza vaccine. If you are currently receiving treatment for CLL/SLL (e.g. ibrutinib, acalabrutinib or venetoclax), you may be eligible to participate. Contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #000444-H. Online: bit.ly/3Syr1Aa.



Cutting the ribbon at the newly dedicated scholar house are (from l) NIH distinguished investigator Dr. Michael Lenardo, NIH OxCam cofounder; Stephen McLean, IBRA founding member and chair; Dr. Barbara Alving, FAES board chair and NIH alumna; Dr. Tara Schwetz, NIH acting principal deputy director; Dr. Ralph Korpman, executive vice president and chief scientific officer of UnitedHealth Group and IBRA director; Nancy El-Hibri, wife of the late IBRA founding director Fuad El-Hibri; Randi Balletta, IBRA president; and Christina Farias, FAES CEO and executive director.

PHOTOS: BETH CALDWELL/BETH CALDWELL PHOTOGRAPHY

SCHOLAR HOUSE DEDICATED

New FAES Residences Offer Homes to Intramural Scientists

The Foundation for the Advanced Education in the Sciences dedicated the first of six new scholar houses to honor supporters of biomedical enterprise and education. The house—5209 West Cedar Lane—was named the “International Biomedical Research Alliance Founders’ House” in an outdoor ceremony on Sept. 13. The new designation recognizes IBRA, a not-for-profit organization whose mission is to invest in and accelerate the development of future leaders in biomedical research, for its guidance and support of jointly trained exceptional research students pursuing their Ph.D. between NIH and the Universities of Oxford and Cambridge.

The event brought together IBRA founding members, chair Stephen McLean and treasurer Alan Jones, as well as members of its board of directors and members of the FAES board of directors and dozens of other distinguished guests.

A highlight was the unveiling of the dedication plaque, to be installed in the foyer of the house,

honoring NIH OxCam cofounder Dr. Michael Lenardo and IBRA founding director Fuad El-Hibri. Their belief that FAES could make a significant contribution to the NIH community by constructing housing for graduate students in close proximity to the campus was unyielding.



Schwetz (l) and FAES CEO and Farias (r) speak at event held under a tent along Cedar Lane.



NIH acting principal deputy director Dr. Tara Schwetz, FAES CEO and executive director Christina Farias and FAES board chair and NIH alumna Dr. Barbara Alving provided remarks. A ribbon cutting followed the ceremony with tours of the new scholar house and networking with fellows



FAES’s Lisa Rogers unveils the plaque heralding the house’s new name.

in the NIH Oxford-Cambridge Scholars Program, some of whom are occupants of the house.

FAES, the nonprofit education partner to NIH, has offered academic programs as well as networking and cultural events since its founding in 1959. The organization supports intramural scholars with essential services, including housing and health insurance, during their research programs at NIH.

FAES owns 5 acres of land across West Cedar Lane from the NIH Bethesda campus and a separate 1.5-acre parcel at the intersection of West Cedar Lane and Old Georgetown Road, where the FAES Social & Academic Center is located.

FAES initially acquired residential property from NIH alumnus and Nobel Laureate Christian B Anfinsen, Jr. His home is now the new scholar house 5205 West Cedar Lane. Dr. Anfinsen was one of 11 NIH scientists to cofound FAES, and he deeded his home and property to the organization.

In July 2021 FAES demolished 4 single-family homes on the property to make way for 6 new dwellings that would provide turnkey accommodations for NIH fellows and trainees.

The new scholar houses are approximately 4,000 square feet, fully furnished with kitchen items, paper products, and cleaning service provided. The residences include 5 private bedrooms each with an in-suite bathroom, 5 storage closets, and 5 individual refrigerators numbered for occupants to make transitions seamless for scholars at the start or end of their lab rotation and stays in Bethesda.

The houses opened to occupants in August 2022 and are nearly 100 percent occupied.

FAES plans to build additional dwellings along Cypress Avenue at the northern part of its property with a goal to increase from 30 to 65 new units for NIH fellows. [R](#)



A view of the back of four new FAES houses along Cypress Avenue