

'MINI-GUT' MAKERS

Pioneer in Field Describes Industrious Organoids

June 10, 2022

Vol. LXXIV, No. 12

BY AMBER SNYDER

Mini-guts. Organoids. It sounds like something out of science fiction, but these terms are part of researcher Dr. Hans Clevers's everyday vocabulary. And these innovations are revolutionizing the way we treat cancer and other diseases.

Clevers, who is an M.D.-Ph. D. professor of molecular genetics at Utrecht University and principal investigator at Hubrecht Institute in the Netherlands, presented an overview of his research in a lecture titled "Organoids to Model Human Disease."

Described by others as a pioneer in the field of organoids, Clevers and his team

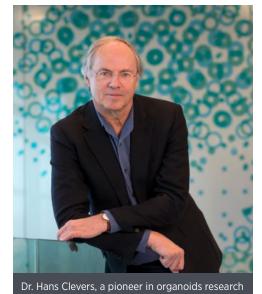


PHOTO: HUBRECHT INSTITUTE

stumbled across their discoveries "more or less by chance," he admitted.

First, Clevers spent some time studying

a family of signaling molecules known as the Wnt pathway, which are important for immune response, as well embryonic development and tissue repair. Most importantly to his work, he learned, "Wnt in the gut is a driver of normal and cancerous stem cells."

Stem cells in the gut? Turns out, most tissues in the human body contain a small number of stem cells, which replace other mature cells that have reached the end of their life cycle.

Inside Crypts

In the intestines, for example, stem cells originate from specialized cells in the epithelium (which form the lining of the digestive tract as well as our skin cells). The intestinal epithelium contains many types of cells, including tiny hair-like structures called villi, which help absorb nutrients from the food we eat, and crypt cells, which sit between the villi and churn out stem cells.

SEE ORGANOIDS, PAGE 4

FOR ALL AGES

Expert Gets Us Talking About the Generations

BY DANA TALESNIK

"I'll bring in new ideas," thinks the fresh-faced Generation Z employee. "I know best. I've been doing this job for 30 years," mutters the baby boomer. "Yeah, that's the



Lynne Lancaster

problem," thinks the millennial.

Multiple generations are showing up at work, each with different experiences, mindsets and aspirations. At times, the tension is palpable in office interactions and

SEE **GENERATIONS**, PAGE 6

HOME ALONE

Consider Canine Separation Anxiety as You Return on Site

BY AMBER SNYDER

Returning to work on site is an adjustment for everyone, but have you considered how your furry friends will handle the change? Roughly 20 percent of dogs experienced separation anxiety pre-pandemic and vets estimate that number to be higher now that people are returning to in-person work.

SEE CANINE, PAGE 8



Jax and his buddy, Alvin Maker of NIH



'Great Road Trip' pays NIH a call. See story, p. 9.

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Andridge To Present 'Methods' Webinar, June 17

The NIH Office of Disease Prevention will present a Methods: Mind the Gap webinar with Dr. Rebecca Andridge on imputation methods for group-based interventions. This webinar will take place on Friday, June 17 at 2 p.m. ET.

Many types of interventions are delivered in groups. Designs to evaluate such interventions include cluster randomized trials (CRTs), individually randomized group treatment trials and stepped wedge CRTs.

In this presentation, Andridge will review strategies for imputation in clustered designs, including the illustration of implementations in software.



Andridge is an associate professor in the Division of Biostatistics at Ohio State University College of Public Health. Her research is focused on imputation methods for missing data, primarily in large-scale probability samples and group randomized trials.

Registration is required. Register at https://bit. ly/3yZqF8o. The webinar will be recorded and available on the ODP website within approximately 2 weeks.

The webinar series explores research design, measurement, intervention, data analysis and other methods of interest in prevention science. For more information, visit prevention.nih.gov/MindTheGap.

FEVS Now Open through July 22

The 2022 Federal Employee Viewpoint Survey (FEVS) is currently open and will close on Friday, July 22. The anticipated government-wide survey is managed by the Office of Personnel Management (OPM) and gives eligible federal employees an opportunity annually to provide confidential feedback about their work satisfaction, organization and its leaders and work/life balance.

In the past few years, participation in the FEVS

2022 FEDERAL EMPLOYEE VIEWPOINT SURVEY

SHARE YOUR FEEDBACK BY JULY 22ND

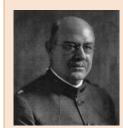
PBS Series Features NIH Origins

NIAID's Dr. David Morens (shown, r) is a featured speaker in PBS's documentary *American Experience: Plague at the Golden Gate* (Season 34, episode 4).

Viewers can "discover how an outbreak of bubonic plague in 1900 set off fear and anti-Asian sentiment in San Francisco," according to PBS's website.

The program "tells the gripping story of the race against time by health officials to save the city from the deadly disease."

PBS Signin



The episode describes the late NIH director Dr. Joseph Kinyoun (shown, I), founder of the Hygienic Laboratory, the nation's first federal laboratory for medical bacteriology that became the National Institutes of Health. In 1900, Kinyoun confirmed the first U.S. case of bubonic plague in San Francisco.

The installment first aired on May 24 during Asian American Pacific Islander Heritage Month and will be available through June 21. For more information, see: https://www.pbs.org/wgbh/americanexperience/films/plague-golden-gate/.

has grown by almost 30 percent as leaders across NIH began to prioritize the survey and its data transparency, making pivotal changes based on employee feedback.

FEVS is available to full- and part-time permanent, non-seasonal employees, on board on or before Nov. 19, 2021. Contractors are not eligible to participate in the survey.

If you are eligible, check your inboxes as well as Junk and Deleted folders for email from OPM with the following header:

From: Federal Employee Viewpoint Survey-HE Subject: [EXTERNAL] 2022 OPM Federal Employee Viewpoint Survey

For more information on FEVS, visit: https://hr.nih.gov/workforce/fevs or email NIHFEVS@nih.gov.

ORF's DEP Updates Waste Disposal Guide

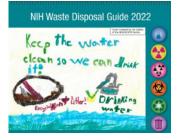
The ORF Division of Environmental Protection (DEP) has revised the *NIH Waste Disposal Guide*.

The guide is a comprehensive, detailed document and foundational tool for managing the different categories of waste generated at the Bethesda campus and the facilities owned and leased by NIH in Rockville, Poolesville, Baltimore, Gaithersburg and Frederick.

The 2022 version of the guide reflects the changes to the current local, state and federal environmental laws and regulations that have occurred since

the previous issuance in 2014.

Hard copies are distributed by the NIH chemical waste contractor



during waste pick-ups and by DEP staff during laboratory compliance inspections. The guide can also be requested and delivered to your lab by calling the Waste and Resource Recovery Branch at (301) 496-7990.

To view an electronic copy of the guide, visit https://nems.nih.gov/environmental-programs/Documents/Waste_Disposal_Guide.pdf.

OPM Announces CFC Special Solicitation for Ukraine Crisis

The Office of Personnel Management has authorized a Combined Federal Campaign (CFC) special solicitation for those affected by the crisis in Ukraine.

The war in Ukraine and the resulting humanitarian and refugee crisis have strained resources throughout Europe and beyond and many of the 2021 CFC charities are working overtime and assisting refugees with food, medical attention, housing and much more.

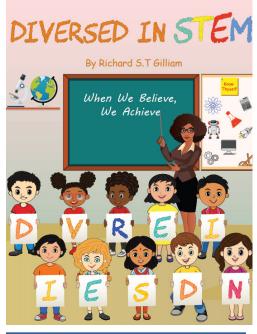
The CFC Giving Portal has reopened for donations and will close on Thursday, June 30, 2022. For details, visit: https://cfcgiving.opm.gov/welcome.

NIH'ers To 'Take a Hike,' June 16

Join the Office of Research Services for Take a Hike Day, a non-competitive and fun walk/run on Thursday, June 16 at 1 p.m. in front of Bldg. 1, rain or shine.

Grab a coworker or two and lace up your walking shoes. What better way to take a break from all the stress of the last 2 years than to go for a leisurely stroll or jog around the perimeter of the NIH campus (total distance of 3.25 miles).

For more information and to register, visit: https://ors.od.nih.gov/pes/dats/wellness/hike/pages/hike.aspx.



At left. Diversed In STEM: When We Believe, We Achieve, a new children's book; above, author Richard Gilliam, a former NIEHS trainee, presented work at conferences and published a paper while at the institute. "It was a great experience along my journey," he said.

is possible," he said.

The teacher in the book encourages the children by helping them embrace their individual interests and talents.

"The book examines how some children might be looked down upon for certain qualities but then reverses that and turns those qualities into something that they can channel into a successful STEM career," Gilliam explained.

She was thrilled to hear about the focus of Gilliam's book.

"The fact that he is encouraging people at a young age, when they are so impressionable, to explore the different kinds of STEM fields out there, and letting them know these careers are for everybody, is such an important message," she said.

Gilliam graduated from Saint Augustine's University in May 2015 with a bachelor's degree in biology. After completing his summer internship with Collins, he worked in the NIEHS Division of the National Toxicology Program with Dr. Jean Harry, a scientist in the division's Mechanistic Toxicology Branch.

Today, Gilliam works as an automation engineer for Eurofins, a global product testing company. In his free time, he volunteers as a mentor with a FIRST Robotics high school team in North Carolina.

Gilliam envisions Diversed In Stem becoming a series.

Former NIEHS Trainee Writes Children's Book About STEM **Careers**

BY JENNIFER HARKER

Richard Gilliam, a 2015 NIEHS postbaccalaureate trainee, recently celebrated the official launch of his new children's book — Diversed In Stem: When We Believe, We Achieve. The author aims to teach children from all backgrounds about careers in science, technology, engineering and mathematics (STEM).

The book features four chapters of learning adventures for Gilliam's fictional fifth grade characters and their teacher. Illustrations show the children practicing various STEM careers as they each imagine future success.

Family background is also explored for each of the children and their personal challenges are turned into promising traits. The book is targeted for readers ages 6 to 12.

STEM for all

Gilliam noted that his slogan "When We Believe, We Achieve" teaches children that success begins with self-belief.

"Especially coming from where I come from-inner city Philadelphia—if you look at the statistics, the odds were never in my favor to be where I am in life right now, so I wanted to show children that anything

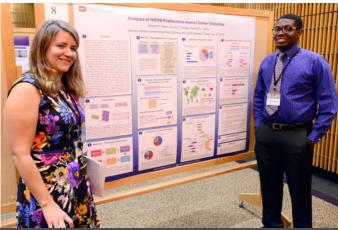
Much of the book is based upon his own life experiences.

"Sometimes, it takes me longer to pick up on certain techniques, but I never give up, and in the time that it takes me to pick up on something, my creativity is activated," he said.

Shaped by NIEHS

Gilliam said his time at NIEHS helped shape this book, which was based on an idea that had been brewing in his mind for several years.

For example, he worked with Dr. Tammy Collins, director of the NIEHS Office of Fellows' Career Development, to assess career outcomes of institute alumni. He documented where postdoctoral fellows landed and what jobs they had after leaving NIEHS. Collins said his work helped shape a career outcome taxonomy that her office still uses.



Dr. Tammy Collins (I) with Gilliam at the NIEHS Summer Internship Program poster showcase in July 2015

PHOTO: STEVE MCCAW/NIEHS



ON THE COVER: E. coli

IMAGE: MARK ELLISMAN AND THOMAS DEERINCK, NATIONAL CENTER FOR MICROSCOPY AND IMAGING RESEARCH, UNIVERSITY OF CALIFORNIA, SAN DIEGO

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The NIH Record



Organoids

CONTINUED FROM PAGE 1

Stem cells are "born" in these crypts and embark on a 2-day journey to the surface. The cells divide and proliferate as they

Single Lgr5 cells form 'mini-guts- in 3D-culture

R-spondin1, EGF, Noggin, in Matrigel

A growth progression of the first "mini-guts" from single stem

travel. As they exit the crypt, they differentiate into one of about 10 different intestinal cell types. Then these newly determined cells travel up the neighboring villi (which takes another 5-6 days) and onward to their destination.

So, where does the Wnt pathway

come into play? Clevers made a groundbreaking discovery in a family of genes involved in the Wnt pathway called TCF, or t-cell factor. TCF regulates the Wnt pathway by deciding which genes are expressed—and those genetic instructions inform stem cells for tissue repair.

cell to organoid

When Clevers was studying one specific factor, TCF4, and its role in colon cancer, he found that malfunctions in the TCF4 gene can cause mutations in stem cells. The malfunctions lead to abnormal cell formation and eventually to development of carcinomas.

DIY Crypts?

When Clevers and his team grew some of these intestinal stem cells in the lab, they made another startling discovery. They expected the stem cells to replicate in the petri dishes and create more stem cells, but instead, "we got epithelial structures," Clevers said.

Given an ideal mix of growth factors, the stem cells had multiplied and differentiated, self-organizing into "crypt equivalents," populated with stem cells as well as the other cell types from the primary epithelium. The stem cells "apparently remember how to build a complete version of the tissue that it [came] from," Clevers realized.

These tiny structures were so similar on a cellular level to the intestine that the researchers dubbed them "mini-guts."

Mighty Organoids

The intestinal organoids were also exciting because Clevers quickly realized they had incredible therapeutic and research potential. They can survive in culture for years without signs of aging. As a final test for the organoids, Clevers and his collaborators grew intestinal organoids from mouse stem

cells and transplanted the organoids into the colons of mice that had inflammatory bowel syndrome (IBS).

The organoids acted like "a living band-aid," said Clevers, by patching over the colon lesions and "fully integrating into the gut tissue." This technology is now being studied in humans with IBS.

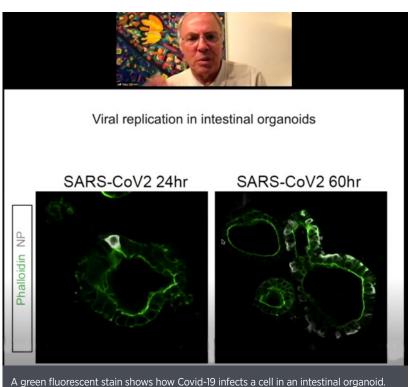
Gut stem cells are the most active stem cells in the human body (the epithelium replaces its cells every 5-7 days), but researchers can also grow organoids from stem cells in other less-proliferative organs.

The procedure is similar regardless of the type of tissue you are trying to grow, Clevers said. The process begins with a tissue sample, which is ground up and put in a medium containing a mixture of growth factors, hormones and other molecules that specific tissue needs to grow. All the cells die, except for the epithelial cells. They contain the stem cells that will regenerate the different types of cells that make up the tissue and ultimately produce organoids.

This technique is used to grow a wide variety of organoids, from pancreas to salivary glands and everything in between. Organoids can also be grown from diseased and cancerous tissue, Clevers said, where "you can measure the drug response in vitro [in a lab-grown organoid] and then show...the patient also respond to the [same] drug."

Multi-Purpose Organoids

In other cases, organoids can be used to study the origin of cancer. Clevers and his colleagues used intestinal organoids to study a genotoxic form of *Escherichia coli* called pks *E. coli*. This common bacterium is found in the microbiomes of about 10 percent of the global human population.





Pks+ *E. coli* contains an extra region of DNA (the pks region) that codes for colibactin, a compound that creates breaks in the host cells' DNA and can lead to new mutations as the DNA repairs itself.

In the study, pks+ *E. coli* induced DNA damage in healthy intestinal organoids. The researchers also exposed organoids to pks+ *E. coli* for 3 months to mimic chronic exposure and then sequenced the DNA of some of the organoids' cells. The team found a unique pattern of mutation that is also seen in about 15 percent of colorectal cancer patients.

Based on this new research, pks+ $\it E$. $\it coli$ could be considered a mutagenic/ carcinogenic bacterium, which may inform preventive measures for patients who are predisposed to colon cancer.

Organoids are also useful in studying infectious diseases.

Clevers collaborated with a team in Rotterdam back in the beginning of the pandemic to study Covid-19. Very little was known about the virus at that time; the researchers wanted to learn more about where and how the virus replicated and what genes might be good drug targets.

Clevers's intestinal organoids came in handy to answer those questions. He and colleagues demonstrated Covid replication in gut organoids and studied some of the genes that are crucial to the virus's infectious cycle. They even identified the transmembrane protein TMPRSS2 (a protein that Covid uses to enter gut cells) as a potential drug target.

Clevers's Covid research with organoids was especially exciting because, he said, "you can essentially read out in human organoids what the virus needs to propagate.

"A large number of studies now are validating organoids as an avatar of patients," he concluded. Possibilities for the technology are exciting and this is just the beginning.

View an archived recording of the lecture at https://videocast.nih.gov/watch=44246.

MANDATORY REPORTING ENABLED

Congress Strengthens NIH Authority Over Harassment at Funded Institutions

Empowered on May 10 by Congress, NIH implemented a general provision in the 2022 Consolidated Appropriations Act (P.L. 117-103) that mandates the NIH director to require NIH-funded institutions report to NIH "when individuals identified as principal investigator or as key personnel in an NIH notice of award are removed from their position or are otherwise disciplined due to concerns about harassment, bullying, retaliation or hostile working conditions."

This provision not only enables mandatory reporting to NIH of removals and disciplinary actions, but also it ensures that NIH is made aware when the reason for the action is concerns of harassment.

Effective July 8, 2022, NIH is requiring notification by the authorized organization representative at NIH-funded institutions within 30 days of the removal or disciplinary

action that must be submitted via a special web form.

"While NIH has made progress

"Wherever NIH research activities take place, our priority will always be to do what we can to eliminate harassment. The passage of this bill into law is an important milestone in support of that vital commitment."

~NIH ACTING DIRECTOR DR. LAWRENCE TABAK

toward our goal of ending harassment in biomedical research, NIH lacked clear authority to require funded institutions to report to NIH whether personnel changes to an NIH grant are related to harassment, only that they should report it," said NIH acting director Dr. Lawrence Tabak, in a statement posted on May 10. "This limited NIH's awareness of when harassment was affecting NIH-supported activities, and therefore NIH's ability to take necessary action to ensure appropriate grant stewardship. That changes today."

Details of the new requirement are posted on https://grants.nih.gov/grants/policy/harassment.htm, a NIH Grants and Funding web page about supporting a safe and respectful workplace at institutions that receive NIH funding and the NIH Anti-Sexual Harassment website at https://www.nih.gov/anti-sexual-harassment.

Once a funded institution reports harassment, NIH will continue to work with the grantee organization, as well as other federal agencies as required, to determine what actions are appropriate.

NIH actions may include approving the institution's substitution or removal of personnel from an NIH grant, restricting award funding, and where neither of these options is available or adequate, suspending or terminating the grant award. Importantly, individuals can continue to report allegations directly to NIH.

"No one should ever have to endure harassment to contribute to biomedical research," Tabak concluded. "Wherever NIH research activities take place, our priority will always be to do what we can to eliminate harassment. The passage of this bill into law is an important milestone in support of that vital commitment. I want to thank all those affected by harassment who shared their stories with NIH, provided input on our efforts to strengthen our policies and practices and held NIH accountable for addressing harassment."

Generations

CONTINUED FROM PAGE 1

may be expressed in subtle or overt ways, from unconscious bias to not-so-silent judgment—the eye rolls, sighs, teeth-gritting anxiety, even outright dismissing others' opinions. Such interactions can leave each generation feeling misunderstood, unappreciated and frustrated.

"Consciously or unconsciously, we do little things that create generation gaps with each other," said Lynne Lancaster, generation expert, management consultant and author.

Lancaster, who has interviewed thousands of workers from each age group, recently delivered an insightful Deputy Director for Management lecture to help reduce the generational divide.

Everyone wants to believe they like all the generations, she said, but the reality is different. There's the old-fashioned traditionalist boss who wants everything printed from the internet to the Gen Zer's puzzlement. Or, there's the baby boomer boss pestered by frequent questions from her millennial employee. She wants a self-sufficient worker; he simply wants more feedback to do the best possible job.

"If we don't communicate, we can drive each other nuts," said Lancaster, who offered tips toward bridging the gaps.

On an organizational level, enhance recruitment and retention strategies. Recruit from a diverse pool and think outside the box, she advised. Is there a younger person ready to step up? Can a bored baby boomer move laterally to a more fulfilling role? Candidly discuss challenges and goals to help cement relationships and retain the best employees.

NIH employees are skewing older, said Lancaster, who researched stats before her lecture. As of January, NIH comprises 1 percent traditionalists (born before 1946); 28 percent baby boomers (born 1946-1964 and also close to retirement); 42 percent Gen Xers (born 1965-1979); 27 percent millennials (born 1980-1994) and 2 percent Gen Zers (born 1995-2012).

"You're going to have a lot of people moving up and out and you'll want to make sure you have the bench strength to replace them as they go," she said.

The same goes for supervisory status. At

NIH Federal Employees with Supervisory Status as of Jan. 1, 2022

Traditionalist Born prior to 1946	Baby Boomer	Generation X	Millennial	Gen Z
	Bom 1948-64	8om 1965-79	Bom 1980-94	Bom 1995-2012
76 (2%)	1351 (39%)	1608 (46%)	457 (13%)	0 (0%)

NIH employees and supervisors are skewing older, said Lancaster. "You're going to have a lot of people moving up and out...you must consider: 'are we grooming people for next steps?"

opportunities for mobility, employees wan

NIH, 39 percent

are baby boomers

are Gen Xers; only

millennials. "You

grooming people

for next steps?"

Beyond

must consider," she said, "are we

of supervisors

and 46 percent

13 percent are

employees want to feel connected. On an interpersonal level, she said, explore ways big and small to foster a sense of belonging. Does everyone feel comfortable speaking up in meetings? Does someone need more coaching?

"Any generation can feel left out or invisible," Lancaster said. "The small ways of being inclusive, even just making eye contact, can help make that connection."

To help reduce misunderstandings among the generations, remember the difference between intent and impact. Something said in the spirit of camaraderie (intent) may get interpreted differently by someone else (impact).

A great example came during the Q&A.

An NIH'er said she gets frustrated every time senior leaders call the organization a family; to her, that implies they're the parents and everyone else is a child.

"An older person meant 'We have each other's backs' and probably never thought family could be a loaded word," Lancaster responded. "Step back, think what the other person means and give him or her a little grace." At the same time, respectfully share concerns. Make others aware if a term has negative connotations to you. "We just can't hear the world through everybody else's ears."

One common thread across all age groups is stress, though the causes usually differ among the generations—from health or financial concerns to caring for dependents.





Show compassion; support each other.

One stress-causing rift at work is: "Everyone should work just like me!" Undo that notion by appreciating where each age group is coming from.

"Each generation arrives into a world of work that's different from the last one," said Lancaster.

Baby boomers are fiercely competitive. They had to compete for that first job and next promotion, so they protect their turf and expect younger generations to pay their dues and stay in their jobs longer too.

Generation Xers, the first generation to emerge from school with tech skills, benefited from a decade-long economic boom that kept hiring them. "Because Gen Xers became this highly valuable commodity, they were able to begin putting pressure on the workplace," said Lancaster. They're the first generation to fight for work-life balance—flexible hours, casual Fridays. They're also skeptical, having

Generation Z is new to the work world, arriving with tech and everything else changing rapidly and having grown up surrounded by social media. "We need to tap into Gen Z to find more ways we can operate

Generations Age Breakdown



effectively in this global, social environment," she said. "They'll lead the way."

Gen Zers want everything to be customizable, from their job duties to their schedules.

To navigate this changing landscape, Lancaster advised setting realistic expecta-

> more authority. "That's how strength, how we get better said, "and it's how people learn."

Appreciate contributes. "I don't know

what we would have done [throughout the pandemic] if we didn't have all five generations [here], with their vast amount of experience, skills, history, technology and institutional knowledge," said NIMHD

executive officer Kimberly Allen.

"What I've learned from interviewing people is we all want the same thing," concluded Lancaster. "Everybody wants to show up at work and do some meaningful work that they care about with co-workers who they like and trust and have their backs. By getting to know the generations, I hope we can achieve that, because we all bring this array of magic into the work we do." B

tions and managing to goals, not to face time or "butts in a chair." Be flexible and delegate

> we build bench as leaders," she

what each group

STANDING UP ARPA-H

Russell Named Acting Deputy Director for New Advanced Research Entity

HHS Secretary Xavier Becerra selected Dr. Adam H. Russell to serve as the acting deputy director for the Advanced Research Projects Agency for Health (ARPA-H), effective June

6. In this role. Russell will lead the intensive process to stand up ARPA-H by continuing to build the infrastructure, business processes and policies, which could take up to a year.

In the coming months, additional interim staff will be brought on



Dr. Adam H. Russell

inaugural director, as the position is presidentially appointed. Public Law 117-103, which was enacted on Mar.

15, authorized establishment of ARPA-H within

HHS. Becerra transferred ARPA-H to NIH on

board while President Biden searches for an

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.

"ARPA-H will have a singular purpose: to drive breakthroughs in health, including the prevention, detection and treatment of diseases such as cancer, Alzheimer's and diabetes," Becerra said, announcing Russell's appointment.

Russell currently serves as chief scientist at University of Maryland's Applied Research Laboratory for Intelligence and Security. He spent a decade as a program manager, first at the Intelligence Advanced Research Projects Activity and then at the Defense Advanced Research Projects Agency.

Russell holds a bachelor of arts in cultural anthropology from Duke University, and an M.Phil. and a D.Phil. in social anthropology from Oxford University, where he was a Rhodes Scholar.

"I don't know what we would have done [throughout the pandemic] if we didn't have all five generations [here] with their vast amount of experience, skills, history, technology and institutional knowledge."

~NIMHD EXECUTIVE OFFICER KIMBERLY ALLEN

grown up inundated with TV commercials in an era of political and corporate indictments. They want to know their organization has their back and will invest in their development.

Millennials carry the stereotype of the entitled generation but they're survivors, said Lancaster. They've already experienced three major recessions in their lifetime. Despite this, they are optimistic and look for meaningful work.

"It's so important when we manage millennials that they understand the difference they're making," she said. And remember, they're not kids anymore; millennials are now between 28 and 42 years old.

Canine

CONTINUED FROM PAGE 1

How can you make your return easier on your dog? NIH Police Sergeant Alvin Maker and veterinarian Dr. Meghan Connolly from the Division of Veterinary Resources weighed in during a recent NIH Employee Wellness Seminar titled "Preventing Canine Separation Anxiety." The lecture was so popular, it was given twice.

Maker is a skilled dog trainer, holding certifications from the Victoria Stillwell Academy, American Red Cross for Dog First Aid and CPR and PetSmart dog training. He also has volunteered at the ASPCA of Anne Arundel County and currently is an adjunct faculty member at the Community College of Baltimore County, specializing in dog obedience training.

Connolly received her degree from the University College Dublin School of Veterinary Medicine. She completed a residency in laboratory animal medicine at Yale University and is currently pursuing a second specialty in animal behavior through the American College of Veterinary Behaviorists.

"Dogs with separation anxiety experience distress when home alone or...separated from their family members," Connolly explained. This can occur even if the dog is in a different room or blocked off by a barrier such as a baby gate.

Separation anxiety may be especially common for so-called "pandemic pets," or animals that were adopted during the pandemic and grew accustomed to their Veterinarian Dr. Meghan Connolly and Ripple

family members being home for extended periods of time.

Separation anxiety may manifest in clear signs of distress such as whining, shaking and panting. Dogs with this condition may also show destructive behavior like chewing on furniture or relieving themselves indoors. Rescue dogs or those who have changed homes multiple times may be more prone to anxious behavior, Maker said, but human behavior also plays a significant role in molding canine conduct.

"Making a big fuss over your dog when you're coming or going [from the house]" can function as a reward for overexcited behavior, Maker said. "Dogs are very connected to human emotion."

Canine Conditioning

This behavior-reward exchange is also

an example of operant conditioning. The core foundation of dog training utilizes two types of conditioning: operant and classical.

In operant conditioning, a learner associates a voluntary behavior with a consequence (positive, negative or neutral). Maker provided the example of his dog Jax, whose adorable begging face will sometimes earn him a bite of Maker's dinner. Begging is a voluntary behavior, and table scraps are a positive consequence. Jax (along with many other cute pups) has learned to associate begging with a food reward.

Classical conditioning is the association of a stimulus with an involuntary response. One famous example is

physiologist Ivan Pavlov's experiment with dogs in which he observed that dogs would salivate in response to a sound when that sound had been paired with a food reward.

"What are some things [you do with] your dog that might classify as classical conditioning?" Maker asked viewers. This can qualify as both intentional and unintentional behavior on the part of the human.

Training is a form of intentional classical conditioning. In clicker training, the dog learns to associate the sound of a "clicker" device with praise. You can also use a visual signal if your dog is deaf or hard of hearing.

What's an example of unintentional classical conditioning? It could be your morning routine before you leave for work. "Whatever you're bringing with you [to work] on a regular basis...are signs or cues or markers that you're about to leave the household," Maker explained. Dogs notice this pattern of behavior and it may be enough to trigger anxiety for your furry friend.

Knowledge is Power

So, now that you know what may be causing stress in your dog's life, how can you prevent or reduce separation anxiety?

Maker reminded viewers to leave and enter the house calmly. You can also "reprogram" certain triggers that you may have unintentionally taught your dog. "Put on your coat, grab your keys [and] go to the living room and watch TV," he advised. This tweak to your routine can help your dog learn that this set of actions doesn't always





Sergeant Maker.

mean that they are going to be left alone.

Training beyond this "reprogramming" can also be beneficial to your dog. Maker set out a checklist for dog owners: identify the problem (i.e., excessive barking), set a goal

(reduce barking), change the situation (don't have the dog in view of the mail carrier) and train for different results. You should also be sure to rule out any underlying health issues that could be causing unwanted behavior.

When trying to curb separation anxiety, a good technique is "independence building," to help your dog learn to be separate from you. Maker teaches this as a sit/stay or down/stay that progresses to the owner being able to leave the room and eventually the house. He recommends using a clicker or a verbal cue such as "yes" or "good" to let the dog know that it has done what you want.

A dog may not know what a clicker means if it has never been trained with one before, but you can "load" the device by clicking it and giving the dog a treat every time he/she looks at you. Eventually, Maker said, the clicker will come to mean: "the behavior you just did was good, so repeat that," and you won't need to reward with a treat every time. If your dog is not food-motivated, you can also use a favorite toy as a reward, or even just verbal praise.

Gadgets and Gizmos

With training, your dog can learn to be comfortable being away from you. Maker also recommended regular exercise such as walks or even playing fetch on the stairs if the weather is poor to work off excess energy. Puzzle toys or other playthings that can have food hidden inside can also be good ways to occupy your pet when you are away.

"It's very important that we exercise our

dogs not only physically, but [also] mentally," Maker emphasized.

Another gadget that he recommends is a "pet cam," or a camera that connects to your phone so that you can observe your dog remotely. It can be used when you are simply in another room and want to observe your dog while you are practicing the "stay" command, or you can use it to check in on your pet throughout the day while you are at work.

An ideal pet cam has the ability to swivel 360 degrees and should be placed in a room

where your dog likes to hang out while you are gone.

Ultimately, Maker said, the goal of the training should be to make your dog realize "they can be in a different space from you and it can be rewarding...They can be comfortable and confident both with you and apart [from you]."

Archived lectures can be viewed at: https://wellnessatnih.ors.od.nih.gov/Pages/default.aspx.

For more resources on training your dog, visit: https://yourdogsfriend.org/.

'Great Road Trip' Visits to Raise Awareness of Kennedy's Disease

The Great Road Trip—a transcontinental journey from Los Angeles, Calif., to Rome, Italy, to raise awareness for Kennedy's disease—stopped by the Clinical Center May 16 to visit with NIH researchers and clinicians who study and treat the disorder.

Kennedy's disease, also known as spinal bulbar muscular atrophy (SBMA), is a rare inherited neuromuscular disorder that causes muscle weakness and atrophy. Currently, there is no cure or specific treatment. Therapy is symptomatic and supportive.

To bring more attention to SBMA and the need for increased research, the road trip team—which consists of members of the Kennedy's Disease Association—is driving a refurbished Citroen 2CV across 2 continents, traveling 6,600 miles from April to July 2022, and stopping along the way for media and fundraising events.



Mark Olimatiek
Citrica, Research Center

On hand to greet the road trip team were several NIH scientists, including many from Dr. Kenneth Fischbeck's laboratory in the hereditary neurological disease section of the **NINDS** Neurogenetics Branch, who are working to develop effective treatments for the disease. Kennedy's disease is caused by a mutation in the androgen receptor gene on the X chromosome.-Shannon E. Garnett









At a virtual event celebrating Asian American, Native Hawaiian and Pacific Islander Heritage Month are Dr. Rina Das (top, I), Dr. Vivek Murthy (top, r), Boston Mayor Michelle Wu and NIMHD director Dr. Eliseo Pérez-Stable.

FAPAC Celebrates Heritage

In observance of Asian American, Native Hawaiian and Pacific Islander Heritage Month, NIH's Federal Asian Pacific American Council (FAPAC) and the National Institute on Minority Health and Health Disparities organized the Dr. Vivek H. Murthy Distinguished Lecture Series for Public Health Leadership. This is the second in a series of fireside chats and lectures in honor of Murthy, U.S. surgeon general.

The goal of the series is to recognize a public health leader whose enduring efforts have made a significant impact on advancing public health.

At this year's meeting, Murthy recognized

Monica Webb Hooper







Dr. Monica Webb Hooper (top, I) moderates the conversation with Murthy and Wu, who shared their personal experiences and described challenges along their career paths—particularly how to cope with mental health issues and cultural barriers for Asian Americans, Native Hawaiians and Pacific Islanders. Pérez-Stable highlighted the important role of public health leaders and NIH in addressing health equity.

Michelle Wu, Mayor of Boston, for her leadership in addressing racism and mental health stigma among the AA and NHPI community.

Dr. Rina Das, president of the NIH chapter of FAPAC, opened the event.

NIMHD director Dr. Eliseo Pérez-Stable highlighted the important role of public health leaders and NIH in addressing health equity. NIMHD deputy director Dr. Monica Webb Hooper moderated the conversation between Murthy and Wu.

The speakers shared their personal experiences candidly, acknowledging key challenges along their career paths—particularly how to cope with mental health concerns and cultural barriers for AA and NHPI.

They discussed the critical importance of addressing health disparities and recognizing issues of loneliness and social connection that are deeply tied to both mental and physical health.

Murthy and Wu highlighted an urgency to rebuild social connection and community. As distinguished public health leaders, both have put tremendous effort into developing new initiatives to rebuild those vital components of a healthy community.

During the Q&A session, the two offered thoughtful insights for next-generation leaders and encouraged them to reach out to other AA and NHPI to boost the visibility of the community.

As the event closed, the message was clear: Collective efforts from everyone are powerful and can lead to a community transformation, with more appreciation for cultural values and history and future opportunities.

The meeting was cosponsored by several organizations, including NIH's Office of Equity, Diversity and Inclusion.

More than 500 people viewed the virtual event, which has been archived and can be accessed at: https://videocast.nih.gov/watch=45154.—Huaying Zhao, Rina Das, Christina Liu, Xinzhi Zhang



NIAMS Communications Director Garrick Retires

BY COLLEEN LABBÉ

NIAMS communications director Dr. Nancy Garrick retired after 28 years of NIH service. The former neuroscientist reflected on a fruitful NIH career, which started earlier than most.

Garrick recalls with fondness her first experience at NIH in 1968 as a teenaged candy striper at the Clinical Center. The volunteer gig seemed like a natural fit, given that medicine was a family affair.

"My father was a medic during World War II and then a hospital administrator, and my mother was a nurse," said Garrick. "I had [medicine and science] in my blood. It was a big deal back then to be a candy striper and it was a lot of fun!" Garrick originally intended to pursue a medical career, but finances did not allow for medical school. She knew she wanted a career in science but wasn't sure what discipline to follow. So she spent some time exploring research careers in biology, biochemistry, physiology and pharmacology, before settling on neuroscience—a field that was exploding in the 1980s and was exciting to her.

"I wanted to really love the science before I pursued a Ph.D. in it," she said, and neuroscience hit the mark for her.

Garrick began her formal NIH career in the NIMH Intramural Research Program (IRP), where she spent 13 years doing basic and preclinical research, first in the Clinical Neuropharmacology Branch and then in the Laboratory of Clinical Science, where she met her late husband, Dr. Dennis Murphy. Garrick then moved to the Office of AIDS Programs in the NIMH Extramural Research Program, where she served as program officer for the institute's neuroimmunology portfolio on HIV/AIDS, which included five AIDS centers.

Garrick took a long break from NIH service in the 1990s and early 2000s to raise her daughter and serve in many volunteer roles at her daughter's school and at church. But once an NIH'er, always an NIH'er, and the call to science remained in her blood.

In 2009, she returned to NIMH, this time as a science writer/editor in the NIMH Office of the Scientific Director, which at the time was headed by Dr. Richard Nakamura.

"I'd known Richard from when we were both IRP researchers," she said.

Two years later, she had an opportunity to join the NIAMS Office of Communications and Public Liaison (now called the Science Communications and Outreach Branch), as its deputy chief. In 2016, she was named branch chief and communications director.

"I've always felt very fortunate to have spent almost my entire career at NIH, but also to have

such a full and varied experience working in the IRP, in extramural and in the NIAMS Office of the Director," Garrick reflected.

The different roles afforded her a unique breadth of institutional knowledge and a holistic perspective on the needs of the agency. Between Garrick and Murphy, who passed away in 2017, they gave more than 78 years of service to NIH.

When asked what she is most proud of, Garrick notes that she has always strived to give back—to support colleagues and staff in their careers and to help them succeed and advance.

"Like Dennis, [who was well known for guiding young investigators], I took mentoring very seriously because I felt like I myself had been well mentored," she said. "The NIH family has supported me through so many tough times. I have such a high regard for the agency and for virtually everyone I've ever worked with."

Garrick sums up her long career with satisfaction: "If you're going to be a civil servant, it's such a privilege to do it in the context of advancing medical research. It's the epitome of what public service means."

VOLUNTEERS

Danazol Study Recruits Participants

NHLBI researchers are testing two low doses of danazol on individuals with short telomere disease and bone marrow disease, lung or liver disease. For more information, call the Office of Patient Recruitment (866) 444-2214 (TTY users dial 711). Online: https://go.usa.gov/xnPYm. Refer to study 18-H-0004.

Healthy Women Sought for Study

NICHD is seeking healthy women to compare with women who have experienced implantation failure and/or early or recurrent pregnancy loss. Researchers want to look at the uterine lining, the endometrium, to understand its role in implantation and miscarriage. Contact the Office of Patient Recruitment, (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Online: https://go.usa.gov/xzE5. Refer to 000206-CH.

Adults with Covid-19 Sought

NIMHD researchers are recruiting adults newly diagnosed with Covid-19 (within 72 hours) for a study. This is a remote study with no in-person visits. The study will collect physical health data using a temperature patch and digital wristband that will be provided to each patient. The collected data will be uploaded to an app using a smartphone and will help researchers gain a better understanding of how Covid-19 progresses in patients and its long-term effects in patient groups with different demographics and risk profiles. To learn more, contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@ nih.gov. Refer to study #000315 https://go.usa. gov/x676m.





Bldg. 18 sits empty, awaiting demolition.

PHOTO: DANA TALESNIK



Days later, it took barely an hour for Bldg. 18T to turn into a pile of rubble.

PHOTO: JOSH OLSON/ORF

Lot 18 Will Be Built on Former Lab Site

A lab complex no longer in use was demolished on campus in May and the space is about to be paved over.

"For this project, the buildings we tore down were much more interesting in their heyday than what we're building in their place," said Josh Olson, project officer in ORF's Division of Design and Construction Management.

Bldgs. 18 and 32, an interconnected complex on the south side of campus, were vacated about 5 years ago, deemed no longer cost-effective to maintain. Only a few remnants—shelves, benches, beaker drying racks—had remained of the research once conducted there.

The space is now getting leveled into a paid visitor parking lot, part of the Building for All campaign to ultimately improve research capability and patient access. This new surface parking—lot 18—will offset the loss of visitor parking in lot 4A across from Bldg. 31 that's now designated for patient valet parking while the Clinical Center builds an extension.

For decades prior, the 18-32 complex was the site of vibrant research. The Office of NIH History and Stetten Museum dug into its archives to share the site's rich history.

Bldg. 18, built in 1973, began as a small, temporary lab and animal space

for NICHD's Reproductive Research Branch, then headed by Dr. Mortimer Lipsett—immortalized with a namesake amphitheater in the Clinical Center. The building and its subsequent annex, 18T, would continue to be used by several branches within NICHD for the next 44 years.

Bldg. 32, despite its higher number, was built earlier, in 1958. The original structure was a greenhouse filled with medicinal plants under study by NIMH investigators. In the early 1990s, the greenhouse was torn down and replaced by Bldg. 32T and an annex, 32T-II, used primarily by NICHD in the 2000s.

A notable discovery took place in the 18-32 complex. It's the site where Dr. Eric Betzig and colleagues built the PALM (photo-activated localization microscopy) for which he received the 2014 Nobel Prize for Chemistry. PALM transformed microscopy, allowing investigators to peer into cells on a nanoscale. Betzig tested and refined PALM in the lab of NICHD's Dr. Jennifer Lippincott-Schwartz.

Now, all of that is history. "I think the parking lot is making good use of the area we're freeing up through their demolition," said Olson.

Lot 18 is slated to be completed and open by late summer. The site plan includes a small grassy plaza in one corner where NIH'ers can congregate.

—Dana Talesnik





At left, Dr. Harvey Mudd (r), chief, section on alkaloid biosynthesis and plant metabolism in NIMH's Biochemistry Lab, conducted research in Bldg. 32A, "the greenhouse (above)," for nearly 30 years. In the 1960 image at left, Mudd and colleague Larry Brown were inspecting cacti growing for an impending study. On right, a modern-day view of Bldg. 32T-II shortly before demolition.

