THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

NATIONAL INSTITUTES OF HEALTH • OFFICE OF THE DIRECTOR | VOLUME 28 ISSUE 4 • JULY-AUGUST 2020

NCATS Postbac Poster Day Goes Virtual

BY STEVEN BENOWITZ, NCATS

Like many of us, Alex Renn has had an unexpected crash course in COVID-19, the disease caused by the novel coronavirus behind a worldwide pandemic. Renn, a postbaccalaureate (postbac) fellow at the National Center for Advancing Translational Sciences (NCATS), is part of a team developing and testing "nanobodies," smaller versions of antibodies. Such nanobodies might ultimately play a role in an anti-virus strategy. He presented his team's work on April 20, 2020, at an NCATS annual event that for the first time went online.

With much of the National Institutes of Health (NIH) workforce teleworking for now, NCATS held its Postbac Poster Day this year during three concurrent Zoom sessions, showcasing research conducted by Renn and 20 other postbac fellows who have been receiving training and mentorship from NCATS scientists as part of the NIH Postbaccalaureate Intramural Research Training Award Program. NCATS provides training and career-development opportunities to enhance knowledge, skills, perspectives, and experiences critical for building the translational-science workforce.

On virtual display were projects ranging from new approaches to treating rare diseases to developing drugs that inhibit cancer growth to improving disease modeling.

Renn is a postbac in the NCATS Early Translation Branch. His poster presentation

CONTINUED ON PAGE 12

Cloistered in the Cloister

Taking Refuge During the COVID-19 Pandemic

BY BIJETA PRASAI, NHLBI

CREDIT: COURTESY OF LAYNE RABORN

Of the 10 NIH Medical Research Scholars residing in the old nun's quarters in the Cloister, three decided to stay during the COVID-19 pandemic. Photo taken before the pandemic (from left): Esha Chebolu, Layne Raborn, and Annah Baykal.

The Cloister sheltered nuns for decades. During the COVID-19 pandemic, it sheltered NIH Medical Research Scholars. From 1925 to 1981, the Cloister (Building 60, also known as the Mary Woodard Lasker Center for Health and Science Education) was home to the Sisters of the Visitation of Washington, a secluded order of nuns. Some of them lived in 10 small bedrooms, or cells, on the third floor and shared a bathroom, kitchen, dining area, chapel, library, and classrooms located on various floors in the building.

CONTINUED ON PAGE 6

CONTENTS

FEATURES • |1| NCATS Postbac Poster Day |1| Cloistered in the Cloister |3| Nine Types of NIH Zoom Callers |11| COVID-19 Timeline (May–June) |13| Signaling Proteins As Potential Targets for Novel Antidiabetic Drugs |14| Taking the Conference Hall to the Computer Screen

DEPARTMENTS • |2| Guest Essay: All Lives Are Sacred |4, 5| Training: OITE Wellness Support; Quiet Leavings |8| Research Briefs |10| COVID-19 Research Briefs |16| Colleagues: Recently Tenured |19| Abbreviations |20| Illustration Moment: Capturing a Moment in Time

All Lives Are Sacred

Building Good Relationships With Communities

BY ALVIN D. HINTON, CHIEF OF THE NIH POLICE

The tragic death of George Floyd at the hands of a Minneapolis police officer and subsequent police shootings throughout our country have drawn worldwide attention to the use of force by the men and women from some of the 18,000 law-enforcement agencies in the United States. A main concern is that use of deadly force is disproportionally applied to Black people. I believe that all lives are sacred. But as you might imagine, the attitudes and demographics of police officers reflect the same attitudes and demographics of America—with both its virtues and faults.

During my long tenure as a law-enforcement officer, I have found most of my fellow officers to be honorable and brave people. There are some, however, who have joined law-enforcement agencies to express biased views and exhibit violent behaviors. And there are some who will tolerate actions they don't agree with, just to go along to get along.

It is very disheartening to be lumped in with the officers who disgrace this honorable profession.

I was watching the news recently while a Montgomery County police officer was explaining that recruiting new officers was becoming very difficult and that the retirement rate had increased from approximately one to 20 a month. The problems are most likely due to the unfavorable portrayal of our profession in the worldwide news media.

I personally believe some of the citizens' mistrust of the police is because of a disconnect between the two groups. Law-enforcement agencies need to focus more on community policing, in which officers build relationships within the community and work in proactive partnerships with citizens to identify and solve problems. "I like to think of it as having a bank account of good will with the communities," Dave Mitchell, chief of police at the University of Maryland, once said. "No matter what agency you represent, at some point a withdrawal [against this account] will have to be made, whether you want to or not." The idea is that with enough feelings of good will, community members will trust that the police—even when responding to possible criminal activity—are always acting in the community's best interest.

Chiefs and other law-enforcement agency officials must root out nonconforming cultures in their organizations that violate the constitutional protections of the citizens they serve. Police officers should understand that they must enforce laws equally, even against fellow officers who are abusing the rights of citizens. Officers must understand they will be held accountable for acts of omission as well as acts of commission. Chiefs must do what is right, no matter if they will have to pay a personal price for their actions or decisions.

Having personally commanded many long and stressful events in Washington, D.C., New York City, and Fort Chaffee, Arkansas, I know at times you must relieve officers and even subordinate commanders when they can't be objective and get too emotionally caught up in certain events.

Police agencies must look inward and ascertain if their policies adequately protect the constitutional rights of the citizens they are sworn to protect. Those policies must also be effective in causing the sanctioning or dismissal of noncomplying officers.

Agencies must ensure we are being guardians of all citizens, no matter what their race, gender, and/or station in life. We must be warriors when threats are made, we must be brave when our citizens need to be rescued, and at times we must disregard our personal safety so others may survive.

I am an optimist and believe we can gain our citizens' support and trust if we make the proper investments required to transform our profession. I am pleased to let you know we have some fantastic officers at the NIH. We are all committed to partnering with members of the NIH community to ensure the safety and security of employees, visitors, patients, and contractors and the protection of NIH's research and knowledge assets. ●

Alvin D. Hinton has been the chief of police at NIH's Division of Police since January 2000. He began his law enforcement career with the United States Park Police (USPP) in the Washington, D.C., metropolitan area and later commanded the USPP New York Field Office, Training Branch, and Major Crimes Unit. He also led USPP law-enforcement efforts at the Cuban Relocation Program at Fort Chaffee, Arkansas. He is a graduate of the FBI National Academy, has a B.S. in administration of justice from American University (Washington, D.C.), and an M.S. in management from Johns Hopkins University (Baltimore). Hinton has managed many high-profile events and participated in the transition process for upgrading the security processes for the NIH after the September 11, 2001, attacks.

Nine Types of NIH Zoom Callers

BY LYDIA MERRICK (ARTIST) AND NIH CATALYST STAFF (CONCEPT)

From the Office of Intramural Training and Education

OITE Wellness Support

BY CHARLESICE HAWKINS, OITE

ALTHOUGH DOING RESEARCH requires perseverance and tolerating setbacks, the COVID-19 pandemic has sent the world reeling—especially for NIH trainees. On March 16, the NIH intramural program shifted all non-mission-critical laboratory operations into a maintenance mode, which meant that almost all labs were closed down.

As a result, most NIH employees and trainees began teleworking. Trainees are especially worried about how the interruption might affect their careers. Sure, they can analyze data and write up their research at home, but many may worry about falling behind. They may become overwhelmed by feelings of stress, anxiety, and depression; some are even experiencing "imposter fears" (feeling like a phony). And those who were already worried and stressed out about their work before the pandemic, are suffering even more.

For the past five years, the Office of Intramural Training and Education (OITE) has been offering wellness resources to help trainees build the resiliency needed to succeed in intense high-knowledge environments and throughout life. But some trainees have been hesitant to reach out for help—they may not feel supported and may worry that taking part in wellness activities might mean diverting attention away from the lab and their careers.

Now with the the stress and uncertainties brought on by the pandemic, OITE has vigorously expanded their wellness resources and brought them online. The OITE staff has also been educating PIs about the importance of wellness activities for their trainees. And trainees are being reassured that taking part in wellness activities is essential for their mental health and successful careers. Of course, OITE continues to offer its other services including career counseling and guidance, virtual poster days, and virtual job fairs.

Based on the simple mantra, "To do well, we have to be well," OITE's expanded wellness program offers online activities in the form of workshops and webinars on stress management and other topics; small-group activities; guided meditation; Wellness Wednesday Brown-Bag Lunches; presentations offering practical advice such as "maintaining connections while socially distancing"; and an OITE blog on wellness with posts such as "Job Searching During Uncertain Times," "Keeping Stress from Derailing Your Work and Life," and "Caring for Your Mental Health During a Pandemic."

OITE wellness advisors are leading confidential discussion groups, too. Some discussions are for specific diverse groups including trainees of color, trainees with disabilities, international trainees, trainees with mental-health concerns, and trainees in the LGBTQ+ community. Trainees feel validated and more connected to the scientific community when they can converse with their peers about coping with anxiety, loneliness, career transitions, and other stressors.

OITE also offers online resources to help NIH faculty, advisors, and staff support themselves and their trainees during the coronavirus pandemic—https://www.training.nih.gov/assisting_the_distressed_trainee—and produced a video titled "Supporting Yourself and Your Trainees During the Coronavirus Pandemic," which can be found at https://youtu.be/q6XP3qnvMVA.

Even as staff and trainees slowly transition back to campus, it will be important to continue the conversations about the challenges trainees are facing. OITE will continue to offer wellness resources and advising, career guidance, discussion groups, leadership training, guided meditations, and many other resources.

In order to do well, we must be well. ●

Links:

- **Wellness resources for trainees, including links to recorded webinars on wellness topics:** https://www.training.nih.gov/wellness
- **Contacts for various groups and activities:** https://www.training.nih.gov/contact
- **Resources for trainee supervisors:** https://www.training.nih.gov/assisting_the_distressed_trainee
- **Video "Supporting Yourself and Your Trainees During the Coronavirus Pandemic":** https://youtu.be/q6XP3qnvMVA
- **"NIH Guidance for Staff on Coronavirus":** https://employees.nih.gov/pages/coronavirus/
- **NIH "Wellness Resources" page:** https://employees.nih.gov/pages/coronavirus/wellness-resources.aspx

From the Fellows

Quiet Leavings

BY ALIA PEDERSON, NIDCD

Recently, a colleague from another lab sent a heartfelt goodbye to our all-institute intramural email list. He had just finished his postbaccalaureate fellowship at the National Institute on Deafness and Other Communication Disorders (NIDCD). These postbac fellowships teach future scientific professionals about the benefits and challenges of biomedical research. They are temporary by design. When they end, we must move on.

I thought about his email for a couple of days, although I barely knew him. I liked the way he talked about the community here, how beautiful it is to work with people driven both by cause and by camaraderie. I also appreciated his vulnerability in such a public forum. But I was most moved by what his message *represents*.

His leaving is a public symbol of the many quiet leavings during the pandemic. Quiet leavings abound—the departure of our scientific director (**Andrew Griffith**) and members of his lab; the anticlimactic dissolution of the class of 2020; many friends' transitions to graduate school. Your own life likely contains many more examples. Before the COVID-19 pandemic we were vaguely aware of impending sendoffs within our small institute, if only because they also came with free food. Now, alone in our homes, the leavings have become nearly silent.

Previously, leavings were a happy marker of the passage of time. Transitions in academia co-occur with many of the NIDCD's most beloved traditions—the retreat, the picnic, the arrival of summer interns, and the reliably abysmal performance of team SWAT in the all-NIH softball league. Most of those things (save the NIDCD retreat, which valiantly transitioned online) have been long forgotten in the slog through our stricken spring. My colleague wrote to express gratitude, but his words conveyed an unspoken sadness: "You will return [to campus], but it will not be the same."

Transition, new opportunities, growth—these are beautiful things. Yet it is also a tragedy that the "we" who left campus at the start of the pandemic will not be the same "we" who return when it ends. Quiet leavings, no matter how small, are losses—loss of what was, and loss of certainty in what, and who, will be. The symbolic leaving of this distant colleague exposed my sheltered expectations of future normalcy to the reality of our collective, overwhelming, pandemic-induced grief.

I have been lucky to preserve my employment, health, and sanity during the pandemic. Many are not so lucky and have been suffering and grieving for a long time. Others, such as essential workers, have been laboring days and nights with barely a moment to eat, let alone grieve. Still others are no longer with us, having succumbed to the virus or become collateral damage in a health-care system spread paper-thin. Their loved ones grieve alone. Immersed in all this pain, it is easy to dismiss our fear, our sadness, and our anger, especially when we are privileged in the pandemic's relative scheme of suffering. But without grief, we cannot move forward.

There will be many more quiet leavings in the next few months. Those who remain expect to return to an eerily empty campus. Colleagues we do see will be visibly separate, hidden behind masks and at least six feet away. Many of us will virtually send off close friends during this time, but we may not notice departures outside our immediate circles until we return to campus. And no matter when we return, it will not be the same. We have many big changes to mourn, but we must also grieve the little losses to accept our new world.

Amid our grief, there will be opportunities to step back and marvel at what a terrible, but also extraordinary, time we have survived. Perhaps, this gentle appreciation will bring inspiration for new projects. Perhaps, it will bring nothing but a moment of relative calm. This is still a gift.

My colleague has moved out west to be a horse wrangler. He intends to apply to graduate programs in ecology or wildlife biology. To him, to my dearest friends, and to all the others who must quietly go, I wish the very best. ●

Alia Pederson, who is from Austin, Texas, has been a postbaccalaureate Undergraduate Scholarship Program Fellow since August 2019. She works in the Section on Neuronal Circuitry in the National Institute on Deafness and Other Communications Disorders and studies the electrical properties of sensory cells in the mammalian auditory system.

Cloistered in the Cloister

CONTINUED FROM PAGE 1

CREDIT: COURTESY OF RITA PARLE

From 1925 to 1981, the Cloister was home to the Sisters of the Visitation of Washington, a secluded order of nuns.

The historic building belongs to NIH now, and those tiny dorm rooms are occupied by students in the NIH Medical Research Scholars Program (MRSP), a 12-month residential, research-immersion program for medical, veterinary, and dental students. In the 1980s, a multi-floor apartment wing was added to the original convent for students when the program was run as a partnership between NIH and the Howard Hughes Medical Institute.

There were 50 students in the 2019–2020 MRSP program. Ten resided in the third-floor rooms; the remainder lived in the apartment wing or off campus. In mid-March when the COVID-19 pandemic forced the closure of many NIH labs and offices—and most employees began teleworking—more than half of the scholars left for their homes. Of those who remained, 15 were in the apartments and three in the dorm rooms. They began teleworking and went to their labs in Building 10 only when necessary.

"The third floor of this building has come full circle, from sheltering the cloistered life of 10 Catholic Sisters 100 years ago to sheltering the cloistered life of three female MRSP scholars now," said MRSP academic director, **Susan Leitman**.

The *NIH Catalyst* asked these three scholars—**Layne Raborn**, **Annah Baykal**, and **Esha Chebolu**—to share with us how they were faring during the pandemic. At the time, Raborn and Chebolu were third-year medical students and are now beginning their fourth year; Baykal was a second-year student and is now beginning her third year.

Layne Raborn

Baton Rouge native Layne Raborn, a medical student at Louisiana State University Health Sciences Center (New Orleans), was working under the supervision of **Michael Collins** in the National Institute of Dental and Craniofacial Research's Skeletal Disorders and Mineral Homeostasis Section. Her research involves both clinical and translational aspects of fibrous dysplasia, McCune-Albright syndrome, and tumor-induced osteomalacia.

Fibrous dysplasia is an uncommon bone disorder in which scarlike or fibrous tissue develops in place of normal bone and may be associated with endocrinopathies (diseases of the hormone-producing glands) and skin macules as part of McCune-Albright syndrome (a disorder that affects the bones, skin, and several endocrine tissues). Tumor-induced osteomalacia is a rare disorder of excess fibroblast growth factor–23, resulting in profound bone fragility.

After she completes her fourth year of medical school in 2021, Raborn plans to do a residency in plastic surgery. She also wants to continue doing research and encourages prospective physicians to consider incorporating research into their careers as well. Although Raborn had to stop going to the lab during the pandemic, she had plenty to keep her busy as she wrote up her projects and completed other clinical projects. And she gained some appreciation for what life might have been like for the nuns.

"Within each of our dorm rooms, there is a historical quote from the time when the nuns resided here," she said. "Staying here… when we are limiting our exposure to the outside world has given us an interesting perspective into the lives of the nuns who previously lived here."

Esha Chebolu

Esha Chebolu hails from Watertown, New York, and goes to medical school at the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo (Buffalo, New York). She aims to become an emergency medicine physician after graduation. She works in **David Goldman's** lab at the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and looks at the variations in responses to alcohol use and the associated genetic and clinical implications. Because Chebolu doesn't do any benchwork and mostly looks at clinical data available from questionnaires and medical charts, she was able to continue her research remotely from the Cloister. She is interested in the clinical manifestations of alcohol use and in the factors that may

predispose certain patients to poorer health outcomes including racial and ethnic health disparities, genetic factors, social stigma, and environmental influences.

"The quiet time has been kind of nice in terms of finishing up my projects this year," said Chebolu. "However, I do miss seeing my lab mates, my other mentors at NIAAA, and the buzz of the work environment."

Annah Baykal

Annah Baykal, a student at the University of Oklahoma College of Medicine (Oklahoma City, Oklahoma), worked in **Rebecca Brown's** lab in the National Institute of Diabetes and Digestive and Kidney Diseases and studied rare diseases of severe insulin resistance such as lipodystrophy (abnormal distribution of fat in the body) and insulin-receptor-mutation syndromes to understand the biology of insulin signaling.

During the COVID-19 pandemic, she maintained a routine similar to her pre-COVID-19 one by attending virtual meetings, writing up data, and working on the planning stages of a new project. She even found a way to replace her daily workouts at the nearby YMCA and keep her fitness routine intact.

Now, "I wake up in the morning and work out in our library with a few of the other MRSP students," said Baykal. She enjoyed becoming "somewhat of a part-time trainer, learning how to put together fun, challenging workouts."

All three scholars acknowledged that having to be sequestered in the Cloister was challenging but presented opportunities.

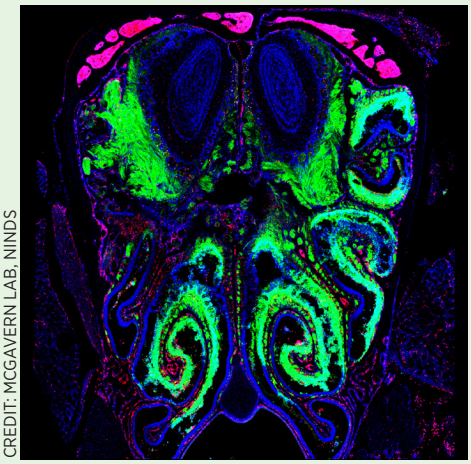
"I know this time has been superchallenging on so many fronts, with transitions and uncertainty, but I'm definitely trying to see quarantine as a time for growth and development in one way or another," said Baykal. "Having the other MRSP students to empathize and go through the loneliness or frustrating times with has only made this year even more unique and life transforming." ●

Most of the 2019–2020 scholars are holding onto their NIH credentials as Special Volunteers so they will still get NIH emails for a few months. The 2020–2021 MRSP class of 51 students is coming to NIH in three groups; each will be onboarded remotely and arrive on campus a few weeks later. The onboarding process will start in mid-July, and all the scholars are expected to be on campus by the end of August.

CREDIT: LAYNE RABORN

Ten of the Medical Research Scholars each lived in a dorm rooms like this one. "In the pre-teleworking period when all 10 of us were in the dorms, sharing a tiny kitchen and bathroom meant we became basically a big family," said Layne Raborn. "We had a wonderful time, made wonderful friendships, and I believe part of that was due to our close quarters." Note the original spiritual message on the upper right wall.

Intramural Research Briefs



CREDIT: MCGAVERN LAB, NINDS

NINDS: The olfactory bulb in the brain is the battleground where viruses (labeled in green) in the nasal passages are stopped from infecting the central nervous system (blue oval structures at the top of the image).

NINDS: NOSY VIRUSES THWARTED BY BRAINY IMMUNE CELLS

NINDS researchers discovered how the immune system protects our brains from infectious agents such as airborne viruses that can enter through the nose. The sensory neurons embedded in the nasal lining give us our sense of smell. These neurons create a conduit to the brain's scent-processing center, the olfactory bulb, posing the risk of airborne pathogens hitching a ride directly to the central nervous system (CNS).

The researchers did experiments in mice and used a fluorescent-tagged vesicular stomatitis virus to see the path a virus takes from the nose to the olfactory bulb. They found a collaborative immune-cell response that mitigates damage to CNS neurons. Unexpectedly, microglia (immune cells within the CNS) face off with the infected sensory neurons in the olfactory bulb and sound the alarm for T cells to respond to pinpoint and destroy the infected cells before they can damage the brain; the microglia remain uninfected themselves.

Understanding this mechanism shines a new light on the significance of microglia in our brain's defense and underscores how their depletion or diminished capacity could open the door for a virus to enter the brain and cause encephalitis or meningitis. Although the virus that causes COVID-19 was not studied, some of its symptoms suggest that the same mechanism described here could be in play, according to NINDS senior investigator **Dorian McGavern**, who led the study. (NIH authors: E.A. Moseman, A.C Blanchard, and D.B. McGavern, *Sci Immunol* **5**:eabb1817, 2020)

[BY EIMEAR HOLTON, NIAID]

NCI-CCR, CC: EFFECTIVE, LESS TOXIC ALTERNATIVE TO STANDARD TREATMENT FOR ADULTS WITH BURKITT LYMPHOMA

A multicenter study led by NIH researchers found that an alternative treatment regimen was highly effective for adults with Burkitt lymphoma across all age groups and independent of HIV status. Burkitt lymphoma is a rare but aggressive B-cell lymphoma that is more common in children than adults. Although the standard dose-intensive chemotherapy (which uses very high doses) can cure the disease, this treatment can be acutely toxic for adults, especially those who are older or who are living with HIV/AIDS. The authors suggest, however, that dose-adjusted (DA) EPOCH-R, which is already used to treat people with diffuse large B-cell lymphomas, is a potentially curative treatment option for elderly patients and those with HIV and other co-morbidities.

In an earlier pilot study with 30 adult patients treated only at NCI, the DA-EPOCH-R regimen was found to be effective. This regimen is tailored to an individual patient's ability to tolerate chemotherapy. To confirm these findings, the researchers conducted a larger, multicenter phase 2 study with 113 patients who had low- or high-risk disease. The treatment was effective across all age groups, including patients in their 70s and 80s, and regardless of HIV status. Furthermore, EPOCH-R can be administered in an outpatient setting, an alternative to the prolonged hospitalization required to receive highly dose-intensive chemotherapy. Further studies are warranted to determine how best to treat patients with CSF involvement. (NIH authors: M. Roschewski, C. Melani, A.N. Lucas, S.M. Steinberg, S. Pittaluga, E.S. Jaffe, R.F. Little, and W.H. Wilson, *J of Clin Oncol* 2020)

[BY MANJU BHASKAR, NINDS]

NINR, NINDS: BIOMARKERS MAY PREDICT RISK OF COMPLICATIONS AFTER MILD TBI

NIH scientists have brought us closer to understanding a neuroinflammatory connection between mild traumatic brain injury (mTBI) and chronic conditions such as post-traumatic stress syndrome (PTSD), postconcussive syndrome (PCS), and depression. In a recent study, investigators at NINR, NINDS, and other institutions identified predictive blood biomarkers in veterans with a history of repetitive mTBI.

Following injury to neural tissue, indicators of cellular damage are released into the blood and exosomes. This study analyzed plasma and exosomal concentrations of inflammatory markers and of neurofilament light chain, a structural protein found in neurons. Researchers then compared biomarker concentrations in a cohort of 195 military veterans enrolled in the Chronic Effects of Neurotrauma Consortium Longitudinal Study among those with no history of TBI to those with one or more mTBIs.

The researchers found a significant correlation between higher biomarker concentrations in veterans with a history of repetitive mTBIs, with length of time in years since the last mTBI, and with increased severity of neurological and behavioral symptoms. "Our findings demonstrate the potential of these easily accessible biomarkers as predictors of behavioral alterations in veterans years after mTBI and provide insights into potential underlying pathologic mechanisms," the authors wrote. (NIH authors: V.A. Guedes, K. Kenney, P. Shahim, B. Qu, C. Lai, C. Devoto, and J.M. Gill, *Neurology* **94**:e2412-e2423, 2020)

[BY MICHAEL TABASKO]

NIA, NIAAA: REPURPOSED DRUG HELPS OBESE MICE LOSE WEIGHT

A study conducted by NIA and NIAAA researchers and others showed that disulfiram, an FDA-approved drug for treating chronic alcohol addiction, normalized body weight, restored insulin responsiveness, and improved liver and pancreas functions in obese middle-aged mice of both sexes.

The nine-month-old mice had been fed a high-fat diet for 12 weeks, and became overweight with signs of prediabetes metabolic problems such as insulin resistance and elevated fasting blood-glucose concentrations. They were then divided into four groups and fed four different diets for 12 more weeks. Mice fed a standard diet normalized their body weight, fat composition, and blood glucose while the mice fed a high-fat diet continued to gain weight and show metabolic irregularities. Mice fed a high-fat diet with either the low- or the high-dose disulfiram also normalized their body weights, insulin responsiveness, and blood-glucose concentrations. The disulfiram treatment also seemed to protect the liver and pancreas from damage.

The researchers are planning future studies, including a clinical trial, to determine the drug's potential in humans. (NIH authors: M. Bernier, S.J. Mitchell, D. Wahl, W. Seo, M. Wang, A. Ali, T. Kaiser, M.A. Aon, E.-Y. Kim, M.A. Petr, H. Cai, C.D. Germanio, A.D. Francesco, K. Fishbein, V. Guiterrez, I.N. Enamorado, Y. Wang, J. Zhang, L. Zhang, R.G. Spencer, K.G. Becker, J.M. Egan, E.G. Lakatta, B. Gao, and R. de Cabo, *Cell Metab* **32**:1–12, 2020)

[BY SUNITA CHOPRA, NCI]

NCI-CCR, NIDDK: NEW BLOOD TEST MAY HELP IMPROVE LIVER-CANCER SCREENING

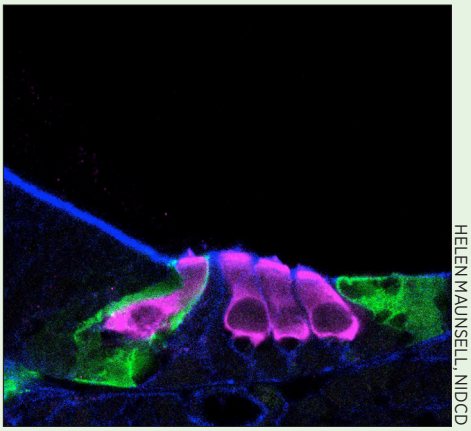
Researchers at NIH and several academic medical centers have developed a new test that may improve the detection of liver cancer before it is symptomatic. They developed a simple blood test to check for a patient's viral infection history. Patients who have suffered from liver infections have a high risk of developing hepatocellular carcinoma (HCC), the most common form of liver cancer. Emerging research suggests that past viral infections may permanently alter how the body fights diseases including cancer.

Drawing on this idea, the researchers assessed how a history of viral exposures in an individual is associated with their risk for developing HCC. They scanned the blood of 899 people, including 150 with HCC, for antibodies from more than 1,000 strains of 206 different types of human viruses. The researchers identified a viral exposure signature (pattern of antibodies)—with "footprints" from 61 different viruses—uniquely associated with HCC patients. To validate the signature, the researchers tested it on blood samples from 173 people with chronic liver disease who were part of a 20-year study. The signature correctly identified the 44 people who developed HCC. It didn't matter whether the blood samples were taken when the cancer was diagnosed or at the beginning of the study, up to 10 years before diagnosis. The scientists plan to test the approach in clinical trials including in a prospective surveillance study of people with risk factors for HCC. (NIH authors: J. Liu, W. Tang, A. Bhudu, M. Forgues, M.O. Hernandez, J. Candia, Y. Kim, E.D. Bowman, S. Ambs, Y. Zhao, B. Tran, X. Wu, C. Koh, P. Surana, T.J. Liang, M. Rajaure, T.F. Greten, and X.W. Wang, *Cell* **182**:1–12, 2020)

[BY THU-LAN LILY NGUYEN, NCI]

NIDCD: DEVELOPMENTAL MAP OF INNER-EAR SOUND SENSOR IN MICE

NIDCD used single-cell RNA sequencing (RNAseq) to developed a roadmap of gene-expression patterns in developing inner-ear cells in mice. The investigators were able to separate 30,000 cochlear cells at four different developmental time points and capture individual cells for analysis with RNAseq.



HELEN MAUNSELL, NIDCD

NIDCD: Single-cell RNA sequencing helped scientists map how sensory hair cells (pink) develop in a newborn mouse cochlea.

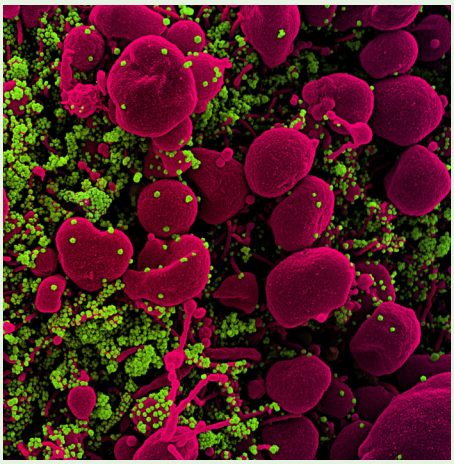
Initially the researchers characterized the cells into types based on expression of known genes in inner-ear cells including inner hair cells, outer hair cells, and support cells. Then they focused on one gene: transforming growth factor beta receptor 1 (*Tgfbr1*), which, when mutated, has been linked to hearing loss in two connective-tissue disorders—Ehlers-Danlos syndrome and Loeys-Dietz syndrome. In mice treated with a *Tgfbr1* blocker during the embryonic stage, the researchers saw fewer outer hair cells than in mice not treated with the blocker, indicating a role for *Tgfbr1* in correct hair-cell development.

Understanding how these cells are formed may one day enable scientists to develop stem-cell therapeutics to treat or reverse hearing loss. The authors have made the RNAseq analysis data available on the Gene Expression Analysis Resource, a web-based platform for sharing and analyzing large datasets. (NIH authors: L. Kolla, M.C. Kelly, A. Anaya-Rocha, K. Ellis, A. Lemons, J.C. Mays, E.C. Driver, and M.W. Kelley, *Nat Commun* **11**:article number 2389, 2020; DOI:10.1038/s41467-020-16113-y)

[BY MEGAN ROEGNER, NIDDK]

Read more briefs and longer versions of these at: https://irp.nih.gov/catalyst/v28i4/research-briefs.

Intramural Research Briefs: COVID-19 Research



CREDIT: NIAID INTEGRATED RESEASRCH FACILITY

NIAID: Colorized scanning electron micrograph of an apoptotic cell (pink) heavily infected with SARS-COV-2 virus particles (green) isolated from a patient sample.

NIAID: REMDESIVIR IMPROVES COVID-19 RECOVERY TIME

The investigational antiviral remdesivir is superior to the standard of care for the treatment of COVID-19, according to a study by NIAID researchers and international partners. In an Adaptive COVID-19 Treatment Trial (ACTT), the researchers compared remdesivir to a placebo in a phase 3, randomized, double-blind, placebo-controlled clinical trial that enrolled 1,063 participants in 10 countries in 58 days. The participants were hospitalized adults with laboratory-confirmed COVID-19 and lower respiratory tract involvement. The authors emphasized that starting antiviral treatments early is necessary to prevent infected patients from progressing to mechanical ventilation. NIAID began the ACTT-2 clinical trial to evaluate remdesivir with baricitinib, an anti-inflammatory drug. (NIH authors: J.H. Beigel, K.M. Tomashek, L.E. Dodd, T. H. Burgess, T. Bonnet, M. Green, M. Makowski, S. Nayak, and H.C. Lane; *New Eng J Med*, 2020; DOI:10.1056/NEJMoa2007764)

[BY FRANCES FERNANDO, NICHD]

NIAID: REPURPOSED VACCINE PROTECTS AGAINST COVID-19 PNEUMONIA IN ANIMALS

In a joint effort between NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana, and others, researchers have shown that a single dose of the investigational vaccine ChAdOx1 nCoV-19 elicits a protective immune response against SARS-CoV-2 pneumonia in monkeys. SARS-CoV-2 is the virus that causes COVID-19. The findings have allowed for the launch of a phase 1 clinical trial in humans.

In both mice and rhesus macaques, there was no sign of virus replication in the lungs; significantly lower amounts of respiratory disease; no damage to lung tissue; no evidence of immune-enhanced disease; and development of spike-specific antibodies to SARS-CoV-2. (NIH authors: N. van Doremalen, J.N. Purushotham, J.R. Port, V. Avanzato, T. Bushmaker, F. Feldmann, J. Schulz, M. Holbrook, A. Okumura, K. Meade-White, L. Pérez-Pérez, B.N. Williamson, R. Rosenke, D. Long, J. Lovaglio, P.W. Hanley, D. Scott, G. Saturday, E. de Wit, and V.J. Munster, *bioRxiv* 2020; DOI:10.1101/2020.05.13.093195)

[BY EIMEAR HOLTON, NIAID]

NLM: KEY GENOMIC FEATURES THAT COULD DIFFERENTIATE SARS-COV-2 FROM OTHER CORONAVIRUSES

A team of researchers in NLM's National Center for Biotechnology Information (NCBI) identified genomic features of SARS-CoV-2, and two other deadly coronaviruses, SARS-CoV and MERS CoV, that distinguish them from other members of the coronavirus family.

The unique features predicted by protein-structure analysis include insertions of specific stretches of amino acids into two virus proteins, the nucleocapsid and the spike. These features are found in all three high-fatality coronaviruses and their closest relatives that infect animals, but not in four other human coronaviruses that are endemic and cause mild symptoms (such as the common cold). The identified features in animal coronavirus isolates could predict the jump to humans and the severity of disease. (NLM authors: A.B. Gussow, N. Auslander, Y.I. Wolf, and E.V. Koonin, *Proc Natl Acad Sci USA* 2020; DOI:10.1073/pnas.2008176117)

[BY MANJU BHASKAR, NINDS]

NCI-CCR, NIAID: POTENTIAL TREATMENT FOR RESPIRATORY DISTRESS IN SEVERE COVID-19

Some patients with severe COVID-19 progress to a hyperinflammatory phase of illness for which there are no proven treatments. NIH scientists and colleagues at other institutions identified the Bruton tyrosine kinase (BTK) protein as a key instigator in this overactive immune response.

Researchers found that some COVID-19 patients in acute respiratory distress show evidence of hyperactive BTK, high blood concentrations of cytokines, and low lymphocyte count. This "cytokine storm," can lead to organ damage and compromise lung function.

In a prospective off-label clinical study, the researchers used the drug acalabrutinib to treat 19 hospitalized COVID-19 patients (11 on supplemental oxygen and eight on ventilators) with severe hypoxia and evidence of inflammation. Acalabrutinib is a BTK inhibitor currently approved to treat severe blood cancers. Most of the patients experienced improved respiratory function, and their inflammation and lymphocyte concentrations normalized. After 10 to 14 days, 73% of those on supplemental oxygen and 25% of those needing mechanical ventilation were discharged to room air.

Targeting excessive host inflammation with a BTK inhibitor has led to a confirmatory international prospective randomized controlled clinical trial. (NIH authors: M. Roschewski, M.S. Lionakis, J.V. Desai, M.A. Zarakas, G. Wright, L.M. Staudt, and W. Wilson, *Sci Immunol* 5:eabd0110, 2020; DOI:10.1126/sciimmunol.abd0110O)

[BY MICHAEL TABASKO]

Read more briefs and longer versions of these at: https://irp.nih.gov/catalyst/v28i4/research-briefs-covid-19.

COVID-19 Timeline at NIH (May–June 2020)

May 4: NIH Clinical Center makes it mandatory for all inpatients to wear surgical masks in their rooms when others are present.

Early May: NIH Clinical Center implements plan to raise the inpatient census and number of outpatient visits. (Elective patients had been deferred since March 10.)

May 7: The NIH-supported Rare Diseases Clinical Research Network launches survey to examine impact of COVID-19 on rare-diseases community.

May 7: NIH Director **Francis Collins** and others testify before the U.S. Senate Committee on Health, Education, Labor, and Pensions on the RADx (Rapid Acceleration of Diagnostics) project to improve testing capabilities and develop new testing regimes for COVID-19.

May 8: NIH clinical trial testing antiviral remdesivir plus anti-inflammatory drug baricitinib for COVID-19 begins.

May 11: NIH Director **Francis Collins** co–authors *Science* commentary stressing the importance of a coordinated strategy to accelerate multiple COVID-19 vaccine candidates.

May 12: NIAID Director **Anthony Fauci** and other members of the White House Coronavirus Task Force testify before the U.S. Senate Committee on Health, Education, Labor, and Pensions.

May 14: The NIAID-funded AIDS Clinical Trials Group begins clinical trial of hydroxychloroquine and azithromycin to treat COVID-19. (The trial is stopped in June because of inadequate enrollment.)

May 15: Five new members of the White House Coronavirus Task Force, including NIH Director **Francis Collins**, are announced.

May 15: NIH Director **Francis Collins** visits White House for an event announcing "Operation Warp Speed," which aims to deliver 300-million doses of a COVID-19 vaccine by January 2021.

May 15: NIAID investigators announce non-peer-reviewed data indicating that an investigational vaccine protects monkeys against COVID-19 pneumonia.

May 18: In a Viewpoint essay published in the *Journal of the American Medical Association*, NIH Director **Francis Collins** & Johnson and Johnson Chief Scientific Officer describe the direction of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), a public-private to address the COVID-19 pandemic.

May 19: Surveillance PCR testing for COVID-19 begins for all inpatients admitted to the Clinical Center for at least one overnight stay, as well as for their approved rooming-in visitors.

May 21: Clinical Center begins performing voluntary weekly surveillance testing for COVID-19 infection in asymptomatic Clinical Center employees.

May 21: Third virtual NIH Town Hall: NIH leadership answers questions about the "NIH Framework to Return to Physical Workspaces"; staff is divided into Groups A, B, C, and D; Group A will return first.

May: NIH sets up "NIH COVID-19 Candidate and Technologies Portal," to collect data on diagnostic, therapeutic, vaccine, other candidates or technologies, and other information regarding COVID-19.

June 5: An NCI study identifies potential approach to treat severe respiratory distress in patients with COVID-19.

June 9: **Deborah Birx**, White House Coronavirus Task Force member, and Jared Kushner, senior advisor to the President of the United States, visit the NIH Vaccine Research Center. (Birx was a fellow in Anthony Fauci's lab in the 1980s.)

June 11: NIH researchers identify genomic features that could differentiate SARS-CoV-2 from other less–severe coronaviruses.

June 15: NIH launches an analytics platform to harness nationwide COVID-19 patient data to speed treatments.

June 16: All of Us Research Program launches COVID-19 research initiatives in an effort to expand data collection that will shed light on the pandemic's spread and impact.

June 19: Fourth virtual NIH Town Hall: focus on safety as staff in Group A start to return to their physical workspaces in some locations.

June 20: NIH halts a clinical trial of hydroxychloroquine to treat COVID-19 because a study shows the drug provides no benefit.

June 20: Because of inadequate enrollment, NIAID stops its clinical trial evaluating hydroxychloroquine and azithromycin.

June 22: NIH employees in Group A return to the physical workspace, except at the Baltimore, Arizona, and North Carolina campuses. Everyone working on campus must wear face coverings, practice physical distancing, and wash their hands frequently.

June 23: NIH investigators and colleagues describe in *mBio* that when the immune system first responds to infectious agents such as viruses or bacteria, a natural brake on the response prevents overactivation.

June 23: More than 300 scientists and clinicians from NIH, other federal agencies, and academia publish a report in *Immunity* identifying steps to expand and improve antibody tests in the COVID-19 response.

June 25: NIH launches a pilot self-assessment reporting tool, using the AlertNIH notification system, for employees who are working on campus to report daily whether or not they have COVID-19 symptoms or have had recent exposure to someone with COVID-19.

June 25: Office of NIH History launches the "Behind the Mask" project to collect stories from all NIH staff regarding the pandemic.

June 26: NIHers were asked to participate in a survey about their willingness to be tested regularly for COVID-19 upon return to campus.

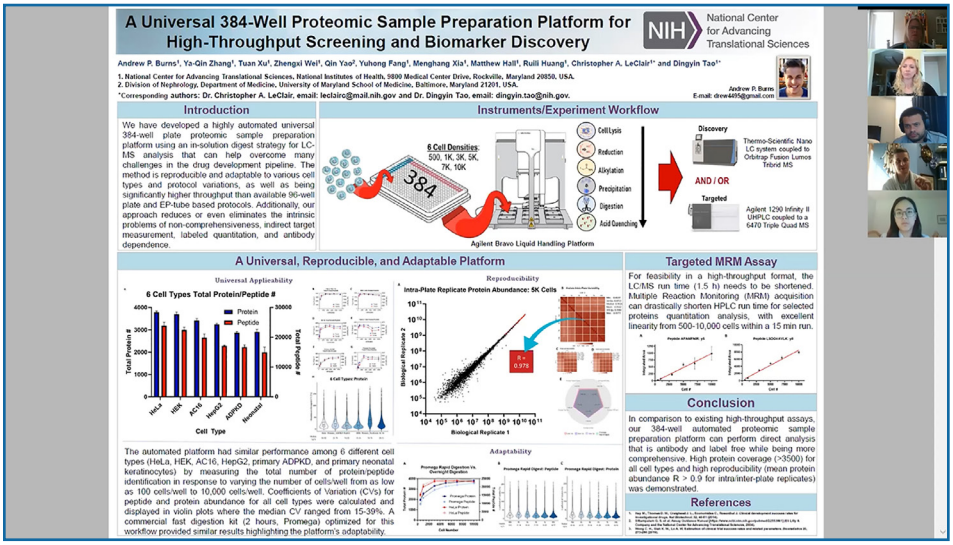
June 30: NIAID Director **Anthony Fauci** testifies at a U.S. Senate Committee on Health, Education, Labor, and Pensions hearing titled "COVID-19: Update on Progress Toward Safely Getting Back to Work and Back to School." He says he is "very concerned" with the increase in COVID-19 cases in some parts of the country and urges the public to wear face coverings. ●

NCATS Postbac Poster Day

CONTINUED FROM PAGE 1

described a state-of-the-art screening technique to develop antibodies effective against SARS-CoV-2, the novel coronavirus that causes COVID-19. Renn showed how SARS-CoV-2 relies on a chemical docking station on the cell surface to infect human cells. That makes the docking station an attractive target for drugs and antibodies.

Renn and his mentors already have identified 10 unique nanobodies that bind to the docking station. While the research is still in its early stages, such nanobodies, if perfected, could eventually be used to prevent or treat COVID-19. The same approach might be useful for other virus-related diseases.



CREDIT: NCATS

During the virtual NCATS Postbac Poster Day, Andrew Burns presented a poster describing the development of a highly automatic universal 384-well plate proteomic sample-preparation platform that performs better than other high-throughput assays and can help overcome many challenges in the drug-development pipeline. The right panel shows (from top): Jessica M. Faupel-Badger (moderator), Patricia Dranchak (judge), Elias Padilha (judge), Burns, and Allison Yang (judge).

Shortening the Diagnostic Odyssey

Several postbac projects focused on rare diseases. Postbac fellow **Ainslie Tisdale** wants to speed up the pace of diagnosing rare diseases. Individuals with rare diseases and their families often go on long, frustrating journeys to get an accurate diagnosis.

Tisdale has been working with the NCATS Office of Rare Diseases Research on an approach to shorten the time required to diagnose and treat rare diseases. In her poster presentation, she described a project examining patient health-care utilization patterns to develop a system for quickly identifying patient needs.

"During the years prior to a correct diagnosis, patients and their families spend large amounts of time, money, and other resources trying to find answers to their and their family member's symptoms," said Tisdale, who also is mentored through the NCATS Division of Preclinical Innovation.

So far, she has evaluated a case study of Batten disease, a group of rare nervous–system disorders, and found a possible profile from common billing codes across centers and collaborators to rapidly identify these patients. Tisdale and her mentors plan to further investigate these profiles and hope their results will lead to the use of artificial intelligence to identify Batten disease sooner.

In a different session, postbac fellow **Danielle Davis** presented a poster on her work studying dystonia—a group of rare neurological disorders characterized by involuntary muscle contractions—which has limited treatment options.

Her project focuses on producing drug-like compounds that can help advance treatment development for a type of dystonia. Davis and her co-workers designed and synthesized a compound that will soon be tested in proof-of-concept animal studies, the first step in testing whether their approach could lead to an eventual treatment. She is planning to wrap up her research over the next several months and apply to medical school.

A New Format To Consider

Event organizers saw the new format as a success. Although the virtual format added technical challenges, "some people told us it was easier to view postbac presentations and participate than in an in-person setting with limited space," said co-organizer **Brittany Haynes** in the NCATS Education Branch. They may consider such a format for subsequent events.

"Many people stepped up to make this virtual event an extraordinary day," said NCATS Education Branch Chief **Jessica M. Faupel-Badger**, who moderated one of the webinar sessions.

Twenty NCATS postbac fellows also participated in the NIH 2020 Virtual Postbac Poster Day held later in April, including as judges. Of the 20, six received Postbac Poster Day Awards, including Renn.

To Tisdale, who plans to pursue a master's degree in public health after a second year at NCATS, the postbac fellowship has been invaluable. "I've been able to interact with experts in the rare-disease community and be trusted with the freedom and opportunity to explore my own hypotheses within the data," she said. "It's been an incredible learning experience." ●

Signaling Proteins As Potential Targets for Antidiabetic Drugs

NIDDK Researchers Shed New LIght on the Mechanisms of Diabetes

BY MEGAN KALOMIRIS, NIAID

A research group led by Jürgen **Wess** in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) recently published three papers that shed new light on the mechanisms of diabetes and show promise for possible treatments. Two of the papers appeared in *Science Advances* and the third was published in *Nature Communications*.

In the first two papers, the researchers discovered two new roles that the signaling protein beta-arrestin-1 (barr1), plays in regulating important metabolic functions. Barr1 is a widely expressed cytoplasmic protein that regulates cellular responses to extracellular stimuli. The researchers used genetically modified mice to observe barr1's effects on metabolism in brown adipose tissue (brown fat) and in certain neurons in the brain.

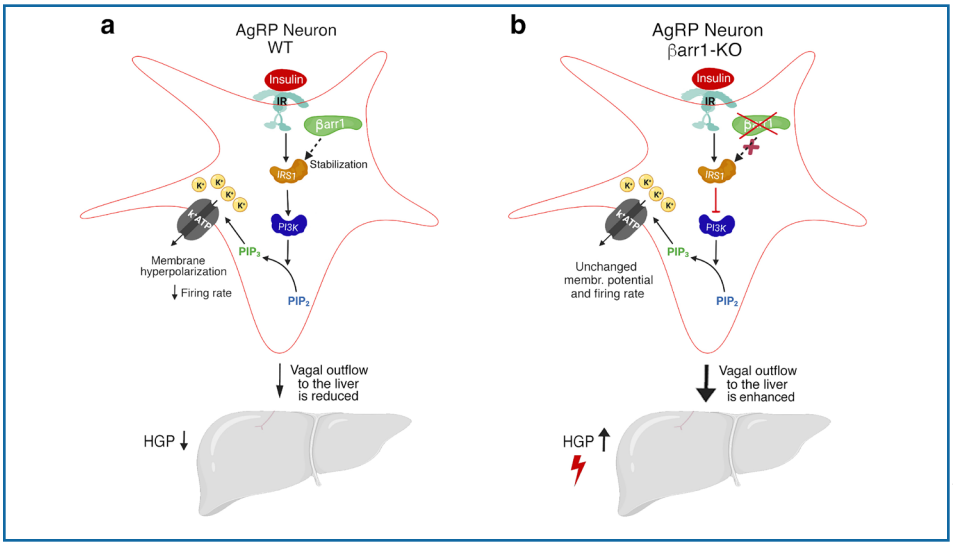
In the first study, Wess's group found that barr1 is critical in maintaining the proper function of brown fat, which metabolizes nutrients to create body heat. The researchers examined metabolic functions in mice that were modified to lack barr1 and in mice that overexpressed barr1 in brown-fat cells. When fed a high-calorie diet, the barr1-deficient mice showed elevated blood-glucose concentrations and developed insulin resistance, two key features of type 2 diabetes; the mice that overexpressed barr1 maintained stable blood-glucose concentrations. (NIH authors: S.P. Pydi, S. Jain, L.F. Barella, L. Zhu, W. Sakamoto, J. Meister, L. Wang, H. Lu, Y. Cui, O. Gavrilova, and J. Wess, *Sci Adv* **6:**eaba1733, 2020; DOI:10.1126/sciadv.aba1733)

"It clearly surprised us that beta-arrestin-1 plays such a critical role in these key metabolic processes," said Wess.

In the second study, the NIDDK researchers demonstrated that barr1 also modulated the activity of hypothalamic agouti-related protein (AgRP) neurons, which regulate food intake and maintain proper blood-glucose concentrations. Mice that lacked barr1 in AgRP neurons displayed impaired glucose tolerance and insulin sensitivity. Mice that overexpressed barr1 in AgRP neurons were protected against obesity-associated metabolic impairments. These effects are similar to those observed with the brown fat barr1 mutant mice, but the difference lies in the mechanism—the presence of barr1 enables insulin to silence AgRP neurons when necessary. The researchers found that barr1's overall effect is to protect metabolic function and stabilize blood glucose, which has implications for treating the harmful effects of type 2 diabetes. "This is the first study demonstrating that [barr1] is essential for maintaining whole-body glucose homeostasis and proper insulin sensitivity," the authors wrote. (NIH authors: S.P. Pydi, Z. Cui, L.F. Barella, J. Pham, Y. Cui, O. Gavrilova, C. Buettner, and J. Wess, *Sci Adv* **6:**eaaz1341, 2020; DOI:10.1126/sciadv.aaz1341)

In the third study, Wess's group demonstrated that the presence of Gi-type G proteins expressed by fat cells is essential for maintaining normal blood-glucose concentrations. "Drug-mediated activation of Gi signaling in fat tissue may prove beneficial for reducing elevated blood-glucose levels in type 2 diabetes," said Wess. (NIH authors: L. Wang, S.P. Pydi, L. Zhu, L.F. Barella, Y. Cui1, O. Gavrilova, and Jürgen Wess, *Nat Commun* **11:**article number 2995, 2020; DOI:10.1038/s41467-020-16756-x)

"Obesity and type 2 diabetes have emerged as major threats to human health in the 21st century," Wess said. "It is essential to develop novel antidiabetic and anti-obesity drugs that are endowed with increased efficacy and show few side effects." ●



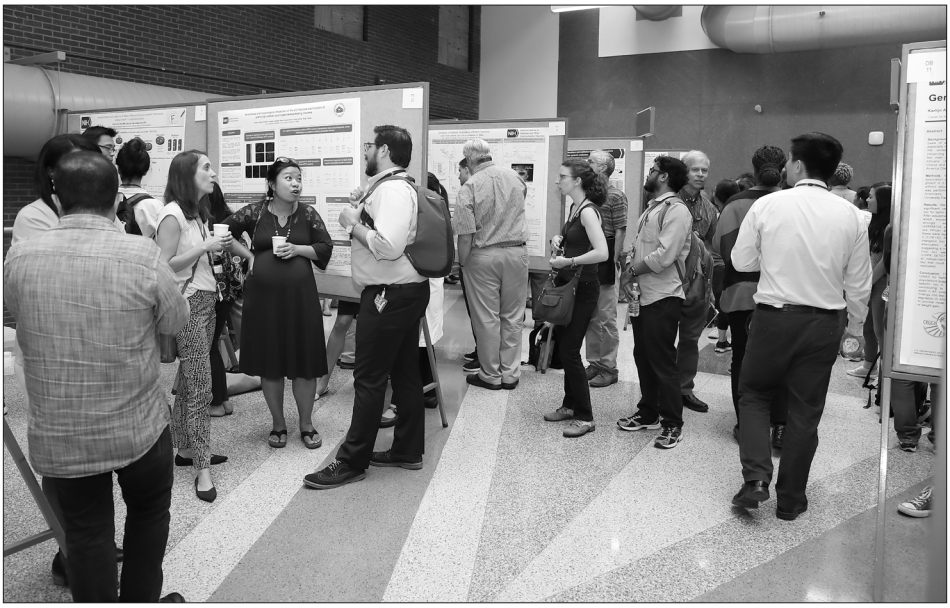
SAI PYDI, NIDDK

NIDDK researchers demonstrated that the signaling protein, barr1, modulates the activity of hypothalamic AgRP neurons. Signals from these neurons help to control glucose production in the liver. Shown: a) The presence of barr1 in AgRP neurons in wild-type (WT) mice reduces hepatic glucose production (HGP) and protects against obesity-associated metabolic impairments; b) Deletion of barr1 in AgRP neurons in knock-out (KO) mice disrupts insulin-mediated neuronal inhibition, ultimately resulting in increased HGP. Key: IR and IRS1, insulin receptors; PI3K is a kinase; PIP2 and PIP3 are membrane-bound lipid molecules; K+ = potassium; K+ATP = ATP-sensitive potassium channel; and vagal outflow represents the vagus nerve sending signals to the liver.

Taking the Conference Hall to the Computer Screen

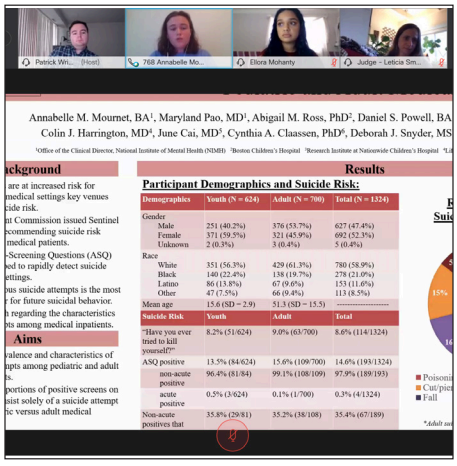
2020 Postbac Poster Day Goes Virtual

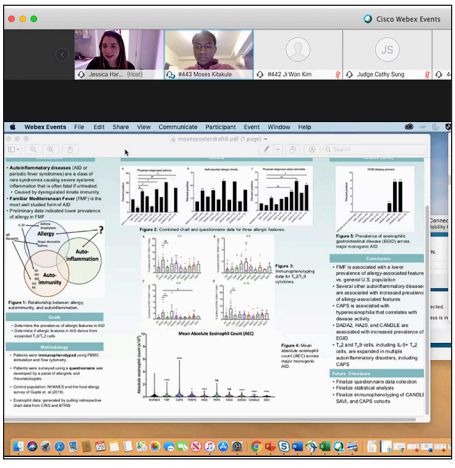
BY MEGAN KALOMIRIS, NIAID

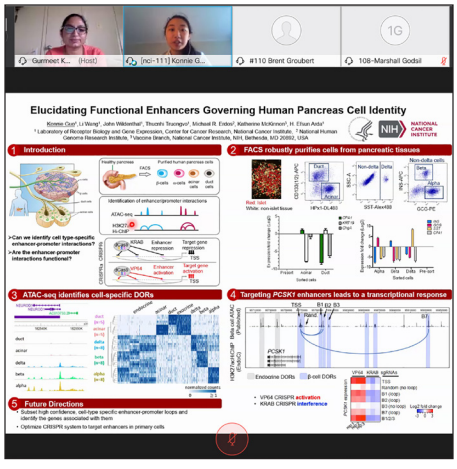


CREDIT: CHIA-CHI CHARLIE CHANG

Will in-person poster sessions, like this one (above) at last year's NIH Research Festival, ever be back? During the COVID-19 pandemic, the Postbac Poster Day went virtual (below). Shown below: some of the virtual poster session presenters and their posters (clockwise from left): Annabelle Mournet, Moses Kitakule, Ugonna Nwannunu, and Konnie Guo.







Postbac Poster Day is a yearly tradition marked by the familiar sight of crowded halls of postbacs, all professionally dressed and eager to share their hard work—via colorful posters—with family, friends, and colleagues. This year, however, as the COVID-19 pandemic spread throughout the United States, sickening more than 1.5 million people, large gatherings of all kinds were prohibited. But thanks to the ingenuity and hard work of event coordinators **Yewon Cheon** and **Virginia Meyer** from the NIH Office of Intramural Training and Education (OITE), the three-day poster day event took place after all—virtually. With the help of the Center for Information Technology (CIT) and weeks of training sessions and practice meetings, Cheon and Meyer magically transformed what would have been a bustling event in Natcher Conference Center (Building 45) into a WebEx teleconference extravaganza with 875 presenters, 345 judges, and 132 virtual "rooms." The event took place April 28–30.

Each "room," or session, could accommodate five-to-seven postbacs, three-to-five judges, and dozens of observers. Like the coordinators, the postbacs and judges rose to the daunting task of dealing with the unfamiliar virtual format.

"Having to present a poster virtually "really challenged me to think deeply about my project and how to explain it as concisely as possible," said **Natalie Hagen** (National Center for Advancing Translational Sciences), whose poster had the complicated title of "UPLC-MS/MS Method Development for Propionyl-CoA [PCC], Methylmalonyl-CoA, and Succinyl-CoA." Translation? She had

helped develop a method to measure the activity of PCC, an enzyme important in energy production, in order to assess the effectiveness of gene therapy in replacing a defective PCC gene. Although Hagen was initially sad when she learned that the traditional, more celebratory, poster day was cancelled, she enjoyed that the virtual format allowed her to hear many of the questions that judges and attendees asked during other poster presentations.

Konnie Guo (National Cancer Institute) presented her project, "Elucidating Functional Enhancers Governing Human Pancreas Cell Identity," which described how cutting-edge genomics techniques have helped identify functional enhancers (noncoding genetic elements) that regulate gene expression among different pancreatic cell types. Guo was initially caught off guard by the unfamiliar virtual format, the five-minute time limit, and the inability to have one-on-one interactions with her audience. She was, however, grateful for OITE's ability to make the poster event happen and the fact that the event was accessible to so many people.

Because she was already preparing for an American College of Medical Genetics virtual meeting, **Ugonna Nwannunu** (National Human Genome Research Institute) wasn't surprised that Postbac Poster Day was going to be virtual, too. Her poster, "Genotype-Phenotype Correlations Among Rubinstein-Taybi Syndrome [RTS] Patients in Diverse Populations," reported correlations and discrepancies between genetic causes and symptoms of RTS (characterized by broad thumbs and toes, short stature, distinctive facial features, and developmental disabilities) in varied populations and geographical regions. Although she missed the interactive nature of a traditional poster presentation, she enjoyed the added feedback from scientists and clinicians who were able to attend because of the convenience of a virtual meeting.

Postbac Poster Day wasn't the first time that **Moses Kitakule** (National Institute of Allergy and Infectious Diseases, NIAID) had presented a poster, but it was the first time he did so virtually. His project, "Systematic Analysis of Allergic Features in Autoinflammatory Syndromes Reveals Disease-Specific Associations," examined the relationship between allergy-associated features and autoinflammatory disease. Condensing his research into five minutes was a little tricky because he wanted to include a lot of background information, but he loved how certain functions on Webex, such as the "zoom" camera setting, allowed him to emphasize sections of his poster.

Having only presented her research in poster format once, **Annabelle Mournet** (National Institute of Mental Health, NIMH) compared the virtual poster presentation to something she likes better—oral presentations and seminars. Her project, titled "Have You Ever Tried To Kill Yourself?: A Comparison of Positive Suicide Risk Screen Responses by Pediatric and Adult Medical Inpatients," concerned the importance of asking questions about previous suicide attempts when screening for suicide risk. Although she prefers giving in-person presentations, she was very impressed by how well OITE transitioned to the virtual format and appreciated that preparing for the presentation led to a richer learning experience overall.

The virtual poster day surprised not only its participants with unexpected benefits and unique challenges, but also the judges. Judges were made up of teams of postdoctoral and clinical fellows, graduate students, staff scientists, and staff clinicians. Traditional poster presentations are noisy affairs with many participants chattering at once, noted one judge, trainee coordinator **Jennifer Patterson West** (NIAID). She found that the virtual format eliminated that issue and allowed judges to focus on their assigned posters. They could ask questions after each presentation, providing postbacs with a chance to further explain their research.

But she and other judges missed some aspects of traditional poster sessions, such as being able to have in-depth conversations with the presenters. Staff scientist **Mark Eldridge** (NIMH) noted the loss of physical cues, such as pointing to the poster to help the audience follow along. (Not all the presenters had discovered the zoom feature that Kitakule used in his presentation.) Postdoc **Courtney Malo** (NIAID) found it difficult to read body language on screen and sometimes was not be able to read it at all when postbacs left their cameras off. Judges note body language while scoring because it is an important component presenters use to engage their audience.

Still, all three judges noted their amazement with the postbacs. "In previous years, the thing everyone had issues with was being clear and concise," said West. But "everyone figured [it out] this time."

Despite the unprecedented circumstances, all the postbacs performed well, and the top 20% received special recognition. The event coordinators were delighted with how everyone came together to help run this event so smoothly. Cheon noted very few technical difficulties and praised OITE and CIT for their assistance. In the end, the virtual format was ultimately a testament to everyone's willingness, flexibility, and ability to adapt to unusual circumstances. ●

Recently Tenured


ELODIE GHEDIN, NIAID


MARKUS HAFNER, NIAMS


MICHAEL J. KRASHES, NIDDK


P'NG LOKE, NIAID


NIKI MOUTSOPOULOS, NIDCR

ELODIE GHEDIN, PH.D., NIAID

Senior Investigator and Chief, Systems Genomics Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases

Education: McGill University, Montreal, Canada (B.S.in biology; Ph.D. in molecular parasitology); University of Quebec, Montreal, Canada (M.S. in environmental sciences)

Training: Postdoctoral fellow, Laboratory of Parasitic Diseases, NIAID; postdoctoral fellow, The Institute for Genomic Research (Rockville, Maryland)

Before returning to NIH: Director, Center for Genomics & Systems Biology, New York University (NYU; New York)

Returned to NIH: In 2020

Outside interests: Cartooning; playing the flute; binge-watching Netflix series

Website: https://irp.nih.gov/pi/elodie-ghedin

Research interests: I am a parasitologist, with expertise in pathogen genomics, specializing in computational and systems biology. My lab and I are studying the parasites and microbes underlying infectious diseases worldwide for the purpose of developing and applying new methodologies to combat these pathogens. In particular, we are focusing on the molecular basis of macroparasite (nematodes) adaptation to niches in their human hosts, and microparasite (virus and bacteria) diversity and interaction in transmission and virulence.

The remarkable persistence of parasitic nematodes, such as *Brugia malayi* (which causes lymphatic filariasis, or elephantiasis) and *Onchocerca volvulus* (which causes river blindness), in chronic human infections suggests the evolution of strategies to regulate and evade host immunity. These organisms may represent a tremendous reservoir of untapped molecules that could be exploited for treating human inflammatory and autoimmune diseases.

In my previous research, my collaborators and I discovered that male worms secrete novel acetylcholine analogs that inhibit the acetylcholine receptor. At NIH, we are testing synthesized versions of these compounds on the cholinergic system of immune cells.

We use a systems-biology approach to understand pathogenesis in severe influenza infection and in COVID-19. We are using new analytical tools to define the genetic structure and mechanisms of evolutionary change in influenza virus and SARS-CoV-2 (the virus that causes COVID-19) within individual hosts over the course of an infection and across chains of transmission. At NYU, I observed that the dynamics of influenza virus evolution are different in high-risk populations such as immunocompromised and obese individuals. At NIH, we are exploring that aspect using an obese ferret model.

I also helped identify several key regulators involved in the host response to influenza virus and bacterial infections, and in host-gene pathways associated with specific antibiotic-resistance genes. At NIH, I will be continuing to explore how the respiratory tract is a potentially important reservoir of antibiotic resistance genes in humans.

MARKUS HAFNER, PH.D., NIAMS

Senior Investigator and Chief, RNA Molecular Biology Group, Laboratory of Muscle Stem Cells and Gene Regulation, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Education: University of Bonn, Bonn, Germany (M.Sc. equivalent in chemistry; Ph.D. in biochemistry)

Training: Postdoctoral fellow, Rockefeller University (New York)

Came to NIH: In 2014 as an Earl Stadtman Investigator in NIAMS

Outside interests: Playing with his three-year-old daughter; cooking; not getting enough exercise; and looking forward to going on the next road trip with his family

Website: https://irp.nih.gov/pi/markus-hafner

ARGYRIS STRINGARIS, NIMH

Research interests: In the RNA Molecular Biology Group, we are studying the impact of RNA-binding proteins (RBPs) on the fate of bound RNA molecules. RBPs are key regulators of posttranscriptional gene expression and control many important biological processes including cell proliferation, development, and differentiation. When RNA regulation goes wrong, the consequences can be devastating and include a wide range of disorders such as cancer, sterility, muscular dystrophy, and many neurological diseases.

We are using large-scale quantitative methods, such as next-generation sequencing and modern mass spectrometry, to determine the functional impact of RBPs on a systems-wide level. Integration of these large-scale datasets allows us to elucidate the function and molecular mechanisms of RNA-binding proteins involved in RNA transport, RNA stability and turnover, and RNA translation.

One recent example that illustrates our approach to dissecting posttranscriptional gene regulatory networks is our study of the RNA-binding protein Dead-end 1 (DND1), which is known to play a role in the development and maintenance of the germline. We found that DND1 may be necessary for the clearance of unwanted RNA in the cells, and that it binds to specific sequences on RNA and recruits molecular machinery that degrades RNA. Mice lacking DND1 develop testicular germ-cell tumors and are sterile. By studying the protein, we think we've found the molecular mechanisms underlying testicular cancer and sterility.

We are also investigating the role of predicted adenylate-uridylate-rich element-binding proteins in determining messenger RNA (mRNA) turnover; identifying and characterizing the interaction network of mRNA binding transport and shuttling proteins and their RNA targets at a sequence and functional level; investigating the impact of select RBPs on translation initiation and elongation; and integrating the results from our systems-level determination of *cis*-acting elements (certain DNA sequences) into high-resolution maps of posttranscriptional regulatory events.

MICHAEL J. KRASHES, PH.D., NIDDK

Senior Investigator and Chief, Section of Motivational Processes Underlying Appetite, Diabetes, Endocrinology, and Obesity Branch, National Institute of Diabetes and Digestive and Kidney Diseases

Education: Boston College, Newton, Massachusetts (B.A. in biology); University of Massachusetts Medical School, Worcester, Massachusetts (Ph.D. in neuroscience)

Training: Postdoctoral fellow, Beth Israel Deaconess Medical Center, Harvard Medical School (Boston)

Came to NIH: In 2013 as a tenure-track investigator

Outside interests: Hiking; running; playing video games; watching trashy reality TV shows

Website: https://irp.nih.gov/pi/michael-krashes

Research interests: The goal of my research is to decipher the brain circuits that underlie hunger. My lab and I are using novel genetic tools and techniques with the hopes of furthering our understanding of how the brain drives humans to obtain food and ultimately how these behaviors can be manipulated to battle obesity and eating disorders.

We are using a rodent model to understand how the brain controls feeding and eating patterns in the procurement of nutrients. We are studying how the brain brings together information sensed from its external environment and its own internal states, including memory, to guide this behavior.

Much of our work focuses on the hypothalamus, which acts to integrate information related to hunger and directs the body toward caloric intake in times of need. We are particularly interested in how this signaling goes awry in models of obesity and in the presence of highly palatable diets such as those rich in fats.

We are currently determining how these diets affect the response of discrete groups of neurons in the brain to food and how these changes lead to the challenges of dieting.

In a recent paper, we highlighted the role of neurons in the paraventricular hypothalamus (PVH), which is critical for appetite regulation. We showed how certain PVH neurons orchestrate acute feeding behavior and demonstrated the indispensability of other PVH neuron types in the maintenance of body weight. (*Cell Metab* **29:**681–694.e5, 2019; DOI:10.1016/j.cmet.2018.10.016)

CONTINUED ON PAGE 18

Recently Tenured

CONTINUED FROM PAGE 17

P'NG LOKE, PH.D., NIAID

Senior Investigator and Chief, Type 2 Immunity Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases

Education: University of Oxford, Oxford, England (B.A. in biology); University of Edinburgh, Edinburgh, Scotland (Ph.D. in parasite immunology)

Training: Postdoctoral training in immunology, University of California, Berkeley (Berkeley, California); postdoctoral training in parasitology, University of California, San Francisco (San Francisco)

Before coming to NIH: Associate professor, Department of Microbiology, New York University (NYU) Grossman School of Medicine (New York)

Came to NIH: In 2020

Outside interests: Swimming; cycling; running; fixing bicycles

Website: https://www.niaid.nih.gov/research/png-loke-phd

Research interests: I am interested in how helminths (parasitic worms) regulate the host immune system. Scientists think that there could be a link between the eradication of helminth infections in developed countries and the epidemic of diseases associated with dysregulated inflammation (such as inflammatory bowel disease, allergy, asthma, and even metabolic diseases such as atherosclerosis and diabetes). One of the reasons I came to the NIH is to develop human challenge studies with these worms, as well as to do detailed immune profiling to better understand whether parasitic worms can be used to treat disease and the mechanisms behind it.

I became interested in this topic when I met and carefully characterized an individual who self-infected with whipworm and was able to put his ulcerative colitis into remission. Using mouse models and studying people in Malaysia, my lab at NYU found that whipworms can reverse dysbiosis (microbial imbalance) by altering the bacterial communities in the gut. However, I also know that there is a lot of interindividual variation in immune responses to these parasites. I am trying to understand the genetic and environmental contributions to immune variation between individuals.

I have also worked with collaborators at Princeton University (Princeton, New Jersey), studying mice in a semirural "re-wilding" facility. These mice had more and bigger intestinal worms than laboratory mice, an immune system that couldn't fight off the worm infection, and a greater range of gut microbiota. Our study suggested that the environment may be the primary driver of the composition of the immune system, while genetics could be a stronger driver of per-cell responsiveness and cytokine production.

My NIH lab and I are also interested in the macrophages induced by these helminths, which have a tissue-repair phenotype termed M2 or are alternatively activated. With these macrophages, the cellular origin determines how they respond to cytokine activation. We are trying to understand the epigenetic and genetic basis for these differences in responsiveness, as well as the heterogeneity of cell states among these macrophages from different cellular lineages.

NIKI MOUTSOPOULOS, D.D.S., PH.D., NIDCR

Senior Clinical Investigator, Oral Immunity and Inflammation Section, National Institute of Dental and Craniofacial Research

Education: Aristotle University of Thessaloniki, Thessaloniki, Greece (D.D.S.); University of Maryland School of Dentistry, Baltimore, Maryland/National Institutes of Health (certificate in periodontics; Ph.D. in immunology)

Training: Intramural Research Trainee Award (IRTA), NIDCR; later became a research fellow and then a clinical fellow

Came to NIH: In 2007 for postdoctoral training; became an assistant clinical investigator in 2010

Outside interests: She is mother of two young children. Reading; cooking; traveling with her family.

Website: https://irp.nih.gov/pi/niki-moutsopoulos

Research interests: My lab's focus is on oral mucosal immunity with an emphasis on aberrant inflammatory conditions of the oral cavity. Over the past few years I have established a bench-to-bedside research program that is aimed at understanding the molecular and cellular basis of oral mucosal immunity in health and in periodontitis, a common inflammatory disease that damages soft tissue in the mouth and can destroy the bone that supports teeth.

In health, the oral mucosal immune system maintains a delicate balance with a rich and diverse community of oral commensals and performs immune surveillance while preventing inflammation. We are interested in how host-microbial interactions preserve health as well as drive chronic inflammatory responses and tissue destruction in the oral cavity. We aim to define key pathways involved in susceptibility to and progression of aggressive forms of periodontitis. In so doing, we hope to identify therapeutic targets.

Our program implements a bench-to-bedside approach. We are leveraging the diverse strengths of the NIH intramural program and interrogating

mechanisms involved in human oral immunity. We supplement this research using relevant animal models and novel immunologic techniques to study tissue immunity. We are working with patients who have rare monogenic immune disorders such as leukocyte adhesion deficiency 1 (LAD1).

LAD1 is associated with severe periodontal bone loss. In working with people who have this rare disorder as well as with people who have common forms of periodontitis, we have identified the upregulation of interleukin-23 and interleukin-17 (IL-23 and IL-17) as potential culprits and therapeutic targets in periodontitis. In fact, our basic research has led to translation into the clinic (in collaboration with **Steve M. Holland's** group in NIAID), targeting the IL-23 response in patients with LAD1. (*Sci Trans Med* **6:**229ra40, 2014; *N Engl J Med* **376:**1141–1146, 2017; *Sci Trans Med* **10:**eaat0797, 2018)

ARGYRIS STRINGARIS, M.D., PH.D., NIMH

Senior Investigator and Chief, Mood Brain and Development Section, Emotion and Development Branch, National Institute of Mental Health

Education: University of Göttingen in Göttingen, Germany (M.D.); King's College London, London (Ph.D. in developmental neuroscience)

Training: Residency in neurology and medicine, University of Göttingen; higher specialist training in child and adolescent psychiatry, Maudsley Hospital (London); research fellow specializing in bipolar spectrum disorders, NIMH

Before returning to NIH: Senior lecturer (tenured), Institute of Psychiatry, King's College London; attending physician, Department of Child and Adolescent Psychiatry, Maudsley Hospital

Came to NIH: In 2008–2009 for training; returned in 2016

Outside interests: Rowing (indoor mainly); studying philosophy; cooking

Website: https://irp.nih.gov/pi/argyrios-stringaris

Research interests: I am interested in how mood is generated and maintained and seek to use this knowledge to improve the treatment of young people with depression and related conditions. I use neuroimaging, epidemiology, and treatment studies (such as cognitive behavioral therapy and medication) to probe brain mechanisms involved in mood and emotion processing. I also have a special interest in reward processing and how it relates to patient's feelings and decision making. A central part of my work is to improve the way we measure mood using multimethod and multisource approaches.

My lab and I did several studies that link depression to aberrant reward processing. In one study, we analyzed functional magnetic-resonance imaging and electroencephalogram studies and found that, when compared with healthy volunteers, depressed individuals showed reduced activation in the striatum, the area of the brain associated with reward responses. These differences may underlie the pathogenesis of depression and have important implications for the development of new treatments for depression. (*Am J Psychiatry* **175:**111–1120, 2018).

In another study, we helped delineate the pathophysiological underpinnings of anhedonia (loss of interest in previously rewarding activities) in children. (*JAMA Psych* **76:**624–633, 2019)

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
DIPHR: Division of Intramural Population Health Research, NICHD
FAES: Foundation for Advanced Education in the Sciences
FARE: Fellows Award for Research Excellence
FelCom: Fellows Committee
FDA: Food and Drug Administration
FNIH: Foundation for the NIH
FNL: Frederick National Laboratory
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCBI: National Center for Biotechnology Information
NCCIH: National Center for Complementary and Integrative Health
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

U.S. DEPARTMENT OF HEALTH AND
HUMAN SERVICES
National Institutes of Health
Building 60, Room 232
MSC 4730
Bethesda, Maryland 20892

FIRST-CLASS MAIL
POSTAGE & FEES PAID
DHHS/NIH
Permit No. G-802
Publication No. 20-6250

Official Business
Penalty for Private Use $300

Printed on at least 20% recycled content paper and can be recycled as office white paper.

CATALYTIC REACTIONS?

If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via e-mail: catalyst@nih.gov; fax: 301-402-1434; or mail: *The NIH Catalyst*, Building 60, Room 232.

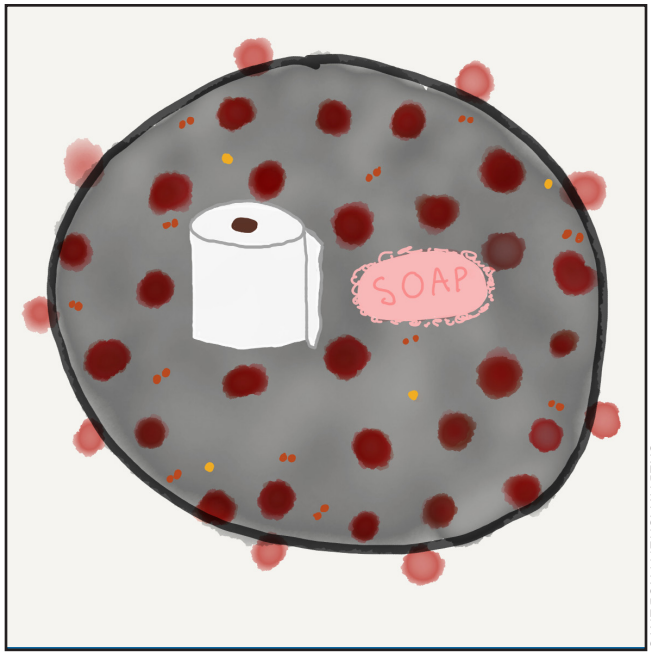
Also, we welcome "letters to the editor" for publication and your reactions to anything on the *Catalyst* pages.

READ MORE ARTICLES, AND EXPANDED VERSIONS OF THE ONES IN THIS ISSUE, ONLINE AT https://irp.nih.gov/catalyst/v28i4.

ILLUSTRATION MOMENT

Capturing a Moment in Time

This drawing is by 10-year-old Ashlyn Roberts, daughter of **Jackie Roberts**, the WALS coordinator in the Office of Intramural Research. Ashlyn's fourth-grade art class was given an illustration assignment to capture a moment in time during the coronavirus pandemic. She wanted to draw the virus itself as well as the things that everyone needed to stay healthy and clean. Ashlyn will be in fifth grade this fall and hopes that her school will start having in-person classes again instead of the virtual classes she's been taking since March 16. ●



CREDIT: ASHLYN ROBERTS

The NIH Catalyst is published bimonthly for and by the intramural scientists at NIH.

Address correspondence to:
Building 60, Room 232, NIH
1 Cloister Court
Bethesda, MD 20892
Ph: 301-402-1449
Fax: 301-402-1434
e-mail: catalyst@nih.gov

The NIH Catalyst online:
https://irp.nih.gov/catalyst