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Itching for Answers

BY CATHERINE EVANS, NIDCR

Why do we itch? Most of us are familiar with the nagging, squirm-inducing sensation, whether from a scratchy sweater, a bug bite, or sunburn. Usually, itch is a fleeting annoyance. But in some conditions, such as psoriasis or during healing of severe wounds, itch can become unrelenting and diminish quality of life. Existing treatments for chronic itch are not always effective. Recent research by scientists, in the National Institute of Dental and Craniofacial Research (NIDCR), working in different labs with differing expertise, may help explain why. Their findings indicate that not all itch is created equal. Distinct combinations of molecules appear to underlie different types of itch, and treatments tailored to specific kinds of itch may offer more effective relief than a one-size-fits-all approach.

When the skin's protective barrier is disturbed—by injury, an insect bite, or even lack of moisture from dry winter air—the immune system springs into action, mounting a defense against potential invaders and helping to heal the area. Part of this process involves the release of small proteins called cytokines, which help immune cells communicate with each other. Some of these cytokines activate itch-sensing nerve fibers in the skin. The resulting signal is relayed to the brain, where it is perceived as the sensation of itch. But scientists haven't fully understood the exact molecules and mechanisms involved.

Scientists in the lab of NIDCR Senior

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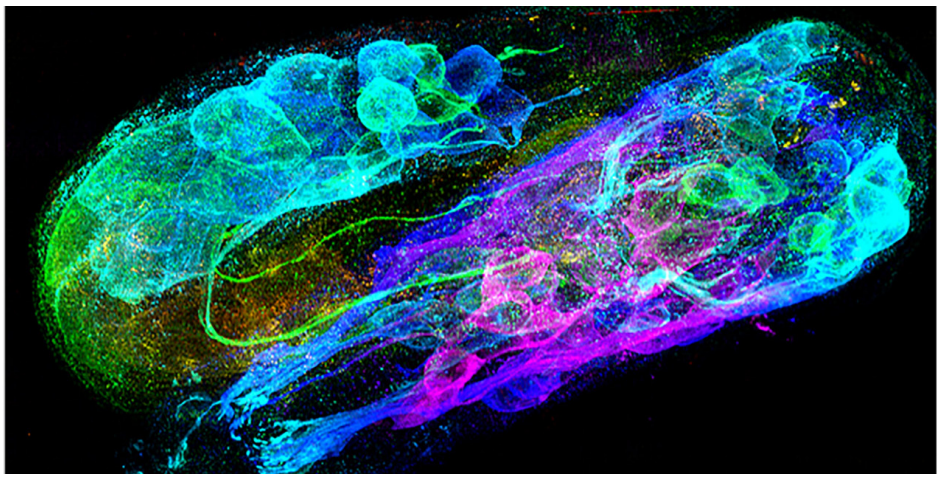
Meet the Makers

NIH Biomedical Engineers Shape Tomorrow's Technology

BY MICHAEL TABASKO, OD



CREDIT: YICONG WU, YIJUN SU, NIBIB

Triple-view scanning confocal super-resolution image of a *C. elegans* embryo stained with fluorescent antibodies to highlight the neuronal structures.

The unassuming salamander has the remarkable ability to regenerate a lost limb. Could we ever regenerate tissue that way or even grow new body parts? What might hidden biological processes happening at the nanoscale teach us about human health? Can mathematical equations be used to understand and predict the behavior of complex biological systems? How can artificial intelligence be effectively used as a tool for biomedical research?

Bioengineers at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) are asking big questions—and striking up trans-NIH collaborations to answer them. These answers hinge on purpose-driven, practical technologies that are just evolving or have yet to be conceived. From advanced optics and artificial intelligence to new imaging techniques, diagnostics, and biomaterials, NIBIB scientists apply the physical sciences

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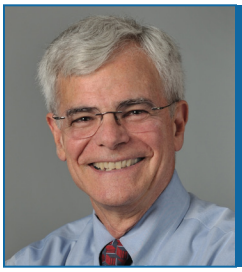


My Time as Deputy Director for Intramural Research: The Recent Years

BY MICHAEL GOTTESMAN, DDIR

In my previous perspective for *The NIH Catalyst* on "The Early Years" of my term as deputy director for intramural research (DDIR), I described how I became DDIR almost 30 years ago, and my initial efforts to sustain an environment strongly supportive of the research and training missions of the intramural research program (IRP). My term began with some substantial changes in the review and oversight of intramural science reflecting the recommendations of the 1994 Marks-Cassell report on the IRP. The changes were mostly related to the role of the boards of scientific counselors (BSCs), the tenure review process, the search process, and the creation of a continuum of training opportunities and career-development trajectories.

In more recent years, there has been a gradual evolution of the IRP to reflect our need to enhance team science, shared resources, and collaborations; build a community of increased diversity, equity, inclusion, and accessibility (DEIA); and strengthen our clinical program including changes in the oversight of the NIH Clinical Center and human subjects research, and paying more attention to the career development of our clinical researchers.

Some of these changes reflect outside reviews of the NIH IRP and the change in NIH leadership. After my initial appointment as DDIR in 1993 by then–NIH Director **Harold Varmus**, I have been privileged to work with two other NIH directors (**Elias Zerhouni** and **Francis Collins**) and three acting directors (**Ruth Kirschstein**, **Raynard Kington**, and **Lawrence Tabak**), all of whom were strong proponents of the IRP. During this period, there were several influential reviews of the IRP, including the 2004 report, the "NIH Director's Blue Ribbon Panel on the Future of Intramural Clinical Research," the 2016 "Red Team" report "Reducing Risk and Promoting Patient Safety for NIH Intramural Clinical Research," and the 2014 Advisory Committee to the NIH Director report on the "Long-term Intramural Research Program (LT-IRP) Planning Working Group Report." What all of these reports have in common was that they were initiated by the NIH director with the intent of ensuring the continuing excellence of research and the research environment at the NIH; they led to important changes in the IRP; and they reflect our absolute commitment to unbiased peer review.

I have become a cheerleader for team science during my term as DDIR. We modified the requirements for tenure at the NIH to include recognition of significant participation in research teams. We created the NIH Director's Challenge Awards to encourage trans-NIH collaborations and shared resources, which complemented the program initiated by then–Clinical Center Director **John Gallin** to support trans-NIH bench-to-bedside translational research activities. The board of scientific directors established the Shared Resources Subcommittee to provide core resources in support of the entire IRP including imaging facilities, training activities, and whole-genome molecular screening. The Collaborative Research Exchange provides a compendium of over 150 IRP cores and commercial resources for use by our scientists. A recent analysis indicated that from 2017 to 2020 approximately 71% of IRP scientists collaborated with scientists in other labs.

It is no secret that the demographics of the IRP do not yet reflect the diversity of the U.S. population. We now have a variety of approaches to improve the DEIA of IRP science. This effort began with programs for the central recruitment of tenure-track investigators (Stadtman Investigator program) and clinical tenure-track investigators (NIH–Lasker Clinical Research Scholars program). More recently, through shared contributions by all of our institutes and centers (ICs) and in cooperation with the first two Chief Officers for Scientific Workforce Diversity, **Hannah Valantine** and **Marie Bernard**, we created an important new cohort program, the Distinguished Scholars Program, to enhance the recruitment of scientists who have demonstrated a commitment to building a more diverse community at the NIH. These programs together have resulted in the substantial diversification of our tenure-track investigators at NIH. Over the past 10 years, the percentage of tenured and tenure-track investigators from under-represented groups at NIH has grown from 4.4% to 8% (and from 4.5% to 19% on the tenure-track alone). The percentage of women scientists at NIH has grown from 23% to 30% (and from 37% to 46% on the tenure-track). The NIH Equity Committee has produced detailed evaluations of diversity efforts in all of our

ICs' intramural programs, resulting in many valuable recommendations that have been embraced by our intramural leadership, including best practices for recruitment of scientific directors and standards for the evaluation of scientific directors, clinical directors, and laboratory and branch chiefs.

Ultimately, an increased emphasis on diversity as an essential component of creative, high-quality science must be embraced by all of our staff. This focus on inclusive excellence will require making achieving diversity a high priority goal for all of our intramural scientists. In addition to the DEIA rating, which is now part of every employee's performance management appraisal program (PMAP), we now require that every BSC review and tenure review include a statement by the principal investigator of the role that they are playing in enhancing DEIA at the NIH.

This century began at NIH with the completion of the new Mark O. Hatfield Clinical Research Center, as part of the overall refurbishment or replacement of close to 50% of our on-campus laboratory and clinical facilities during my time as DDIR. As a physician–scientist, I have paid particular attention to clinical activities at the NIH and the translation of laboratory science into clinical experiments (bench-to-bedside) and the encouragement of bedside-to-bench opportunities to learn more about human biology. The "Red Team" report caused us all to rethink the role of the Clinical Center as the world's premier clinical research institution that also must provide the highest standard of clinical care while ensuring patient safety. Our staff rose capably to this challenge, continuing a proud tradition of excellence in all aspects of research and patient care. With the help of the DDIR's deputy director for intramural clinical research (currently **Janice Lee** who is also the clinical director of the National Institute of Dental and Craniofacial Research), we continue to work to establish appropriate recognition and career progression for our clinical faculty, including staff clinicians, staff scientists (clinical), tenure-track investigators, senior investigators, and senior clinicians. This effort has resulted in a career progression and much better delineated responsibilities for our staff clinicians and opportunities to conduct independent research.

Although the goal is still aspirational, under Janice Lee's oversight with the help of **Andy Baxevanis** and **Yang Fann**, we are developing a Clinical Research Informatics Strategic Plan Initiative to provide interoperable systems for collection, analysis, and sharing of clinical research data. And, of course, after many years of trying to bring change to our human subjects research program, we hired **Jonathan Green** to run the Office of Human Subjects Research Protections. He accomplished what we thought might be impossible: the unification and harmonization of our 12 institutional review boards into one central office.

These accomplishments depended on the outstanding team of NIH scientists and program directors in the Office of Intramural Research. All of my immediate senior staffers have strong backgrounds as working scientists, ensuring a deep understanding of the needs of our scientific staff. I want to express my deep gratitude to my principal deputy director, **Richard Wyatt**, with whom together we share 100 years of NIH experience and nearly every one of my responsibilities; to **Roland Owens**, director of research workforce development; **Arlyn Garcia-Pérez**, director of policy and analysis; **Carl Hashimoto**, director of faculty development; **Charles Dearolf**, director of program development and support; and **Kathryn Partin,** director of research integrity.

My next essay will address challenges and opportunities in the coming years for the intramural program. I will leave these as a bequest to my successor. ●

Links to reports and other items mentioned in this article:

- 1994 Marks-Cassell Report on the IRP: https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/review_science/nih-irp_redbook.pdf)
- The "NIH Director's Blue Ribbon Panel on the Future of Intramural Clinical Research": https://www.genome.gov/Pages/About/NACHGR/2004NACHGRAgenda/Tab H - BlueRibbonPanel.pdf
- The 2016 "Red Team" report "Reducing Risk and Promoting Patient Safety for NIH Intramural Clinical Research": https://acd.od.nih.gov/documents/reports/Red_Team_final_report_4262016.pdf
- The 2014 Advisory Committee to the NIH Director report on the "Long-term Intramural Research Program (LT-IRP) Planning Working Group Report": https://acd.od.nih.gov/documents/reports/ACD-IRP-WG-report.pdf
- Intramural Research Program Personnel Demographics: https://oir.nih.gov/sourcebook/personnel/irp-demographics
- *The NIH Catalyst* DDIR essay on "The Early Years" (January–February 2022 issue): https://irp.nih.gov/catalyst/v30i1/from-the-deputy-director-for-intramural-research
- NIH Equity Committee: https://diversity.nih.gov/programs-partnerships/nih-equity-committee

From the Fellows Committee

Getting to Know Us

BY ALISON JANE MARTINGANO, NHGRI

FelCom members have been meeting virtually since the COVID-19 pandemic began in 2020.

Are you an NIH postdoc or clinical fellow? Do you have an idea, or an issue, or just want to meet fellows outside of your own institute or lab? The NIH Fellows Committee (FelCom) is here to represent you. FelCom is NIH's local postdoc association (you may be more familiar with these groups from university campuses). I recently spoke with FelCom Clinical Fellows Co-chair **Marja Brolinson** (National Institute of Child Health and Human Development) and FelCom Basic Science Co-chair **Vasty Osei-Amponsa** (National Cancer Institute) to find out how FelCom seeks to improve the training experience of all fellows.

"FelCom plays a vital role at NIH," said Brolinson. "It serves as the voice of postdoctoral and clinical fellows and functions as a wealth of knowledge, experience, and connection for all fellows at NIH."

FelCom comprises postdoctoral representatives from each of NIH's 24 institutes and centers (ICs) that have intramural programs (NIH has 27 ICs, but not all of them have intramural programs.) FelCom representatives meet once a month to share ideas for improving the fellow experience and raise concerns with relevant subcommittees and FelCom liaisons. **Lori Conlan** from the Office of Intramural Training and Education and **Charles Dearolf** from the Office of Intramural Research also join Felcom meetings to share information and to hear and discuss the concerns of fellows.

But you don't have to be an official representative to attend FelCom meetings. All fellows are welcome—and encouraged—to attend monthly meetings.

Building a community

"I believe FelCom presents a great opportunity to build a community," said Osei-Amponsa. "Fellows feel comfortable enough to express their concerns as trainees and share their visions for a strong NIH fellows community."

FARE awards

FelCom organizes the Fellows Award for Research Excellence that recognizes the outstanding scientific research performed by intramural postdoctoral fellows. In addition, FelCom organizes events, helps to develop policy, and advocates for fellows within and outside of NIH. Liaisons and subcommittee chairs sit on a variety of internal and external boards to advocate for fellows. For example, FelCom representatives who sit on the NIH Child Care Board have recently been advocating for improved child-care cost support for trainees. FelCom is also represented in a variety of external organzations such as the National Postdoctoral Association.

Interacting with NIH leaders

"FelCom provides the opportunity to interact with leadership at the NIH," said Brolinson, who has sat in quarterly meetings with the director of the NIH Clinical Center to address issues of concern related to clinical fellows.

With fellows rotating in and out of NIH regularly, vacancies occur frequently, giving many fellows the opportunity to serve as liaisons or on subcommittees they care about. Elections for vacant FelCom positions are held at monthly FelCom meetings.

Many ways to get involved

There are many other ways to get involved with FelCom, including attending organized events or joining as an ad hoc (nonvoting) member of one of the subcommittees. Recent events include "International Movie Night" run by the Visiting Fellows Committee, a seminar on "Careers in Data Science" organized by the Career Development Subcommittee, and

"Palentine's Day" run by the Health and Recreation Subcommittee.

"As for me, personally, I joined FelCom through being a co-chair for the Clinical Fellows Committee," Brolinson told me.

"Getting involved in FelCom not only expands your network, exposing you to different opportunities, career- and lifestyle-wise, but it also builds your marketable soft skills," said Osei-Amponsa. Being involved with FelCom "is a privilege that I think all fellows should take advantage of."

Serving as a representative, a liaison, and/or on a FelCom subcommittee can be fun. Why not come to the next FelCom meeting to find out what it's all about? Meetings are held on the first Thursday of every month from 4:00 to 5:00 p.m. and will continue to be virtual for the foreseeable future.

FelCom subcommittees

Consider joining. If the chair position is vacant, you can volunteer to run for election to that position.

- **Career Development Subcommittee:** Organizes a year-long seminar series about how to survive postdoc training and teaches skills needed for making the transition to various professional positions.
- **Clinical Fellows Subcommittee:** Addresses concerns related to clinical fellows, clinical fellowships, patient care, and research at the NIH Clinical Center.
- **Fellows Award for Research Excellence (FARE) Subcommittee:** Organizes the FARE competition to recognize the outstanding scientific research performed by intramural postdoctoral fellows.
- **Health and Recreation Subcommittee:** Promotes health and well-being among trainees; plans and manages activities centered on fitness, self-care, and health habits.
- **Service and Outreach Subcommittee:** Provides an opportunity for NIH Fellows to give back to the NIH and greater Washington, DC, communities.
- **The Mentoring Subcommittee:** Ensures that the mentoring system at the NIH creates strong mentor-mentee relationships that allow fellows to develop and achieve their career goals.
- **Social Activities Subcommittee:** Promotes the social interaction of NIH fellows through organizing a wide variety of networking and social events.
- **Visiting Fellows Subcommittee:** Composed of NIH postdoctoral visiting fellows from around the world, this subcommittee works to make their experience here worthwhile.
- **Wednesday Afternoon Lecture Series (WALS) Subcommittee:** Seeks to improve fellows' participation in the nomination of WALS speakers and to increase opportunities for fellows to interact with speakers. ●

Subscribe to the FelCom LISTSERV for meeting information at https://list.nih.gov/cgi-bin/wa.exe?SUBED1=fellow-l&A=1. For more information about FelCom and how to get involved, go to https://www.training.nih.gov/felcom_officers_and_committee_chairs.

Alison Jane Martingano is a postdoctoral fellow in the National Human Genome Research Institute. Her research involves using virtual reality to evaluate how providers communicate genomic concepts and show empathy during physician–patient interactions. In August, she will be joining the University of Wisconsin at Green Bay as an assistant professor of psychology.

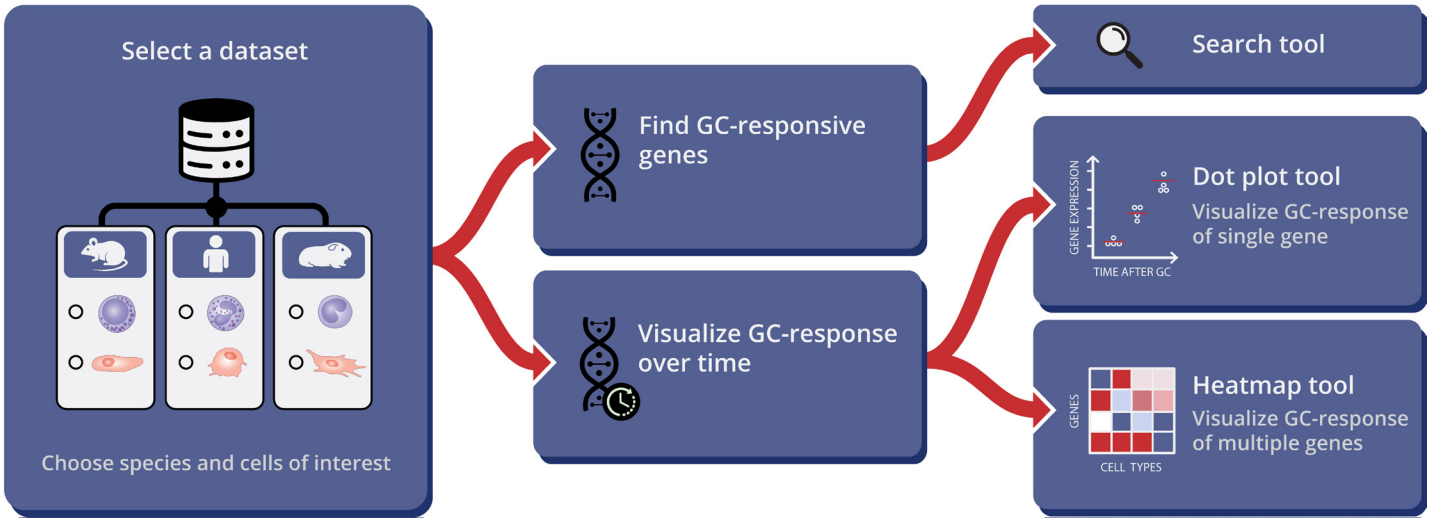
NIH ABBREVIATIONS

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

New Web Application

For Studying Cellular Responses to Glucocorticoids

BY SATABDI NANDI, NIA



CREDIT: MARTYN GREEN, NIAMS

Typical workflow for using the GCgx tool. The user selects a dataset containing cells of interest for a chosen species then searches for GC-responsive genes or visualizes GC-response over time results as a dot plot (for a single gene) or a heatmap (for multiple genes).

Glucocorticoids are a powerful class of steroid drugs used for anti-inflammatory and immunosuppressive therapy and to fight an overactive immune system. During the COVID-19 pandemic, for example, dexamethasone and other glucocorticoids were successfully used to treat patients with severe COVID-19 by mitigating the systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction. But these drugs can also have serious side effects that affect every organ system. Although the drugs have been around for more than 70 years, scientists have a poor understanding of how glucocorticoids regulate the immune system and the mechanisms by which they cause toxicity in different organs. Many important experiments have been performed in cell-culture or animal models. However, recent studies have revealed that each type of cell responds very differently to glucocorticoids, so those findings can't be easily extrapolated to determine how human cells might react.

Now there's a new web tool that will allow scientists to study how different human cell types will respond to glucocorticoids. The tool, called GCgx, was developed by **Luis Franco's** lab at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and scientists at Bioinformatics and Computational Biosciences Branch at the National Institute of Allergy and Infectious Diseases (NIAID). Franco is an Earl Stadtman Investigator and an NIH Distinguished Scholar, and has a secondary appointment at NIAID. The tool is described in the *Journal of Molecular Endocrinology* (*J Mol Endocrinol* **68:**B1–B4, 2022).

"GCgx is a scientific web application that allows investigators to quickly find answers to questions like, 'Are my genes of interest responsive to glucocorticoids in specific cell types?'" said Franco. "If so, how does their level of expression change over time, and how statistically significant are the differences?"

GCgx is a mobile-friendly tool that can quickly display information about the transcriptional response to glucocorticoids from individual cell types. The tool has an extensive dataset that was generated in Franco's lab and is based on total RNA sequencing in nine primary human cell types: B cells, CD4+ T cells, endothelial cells, fibroblasts, monocytes, myoblasts, neutrophils, osteoblasts, and preadipocytes. New datasets will be added over time, based on user input.

"GCgx will make it much easier to share data in a ready-to-query format with the rest of the research community, hopefully enabling better-informed experiments," said Franco.

Researchers can use GCgx's GC-responsive genes search function to determine contrasting gene responses in immune cells versus non-immune cells. GCgx's heatmap function can simultaneously visualize the response to

glucocorticoids across many genes and cell types within a given dataset. In addition, the dot plot function can be used to display the transcript abundance of a single gene of interest before and after glucocorticoid treatment.

"I am glad that Luis and colleagues developed the GCgx tool, because the utility of GCgx will be appreciated broadly by many groups," said Earl Stadtman Investigator **Mia Sung** from the National Institute on Aging. Using published data from Franco's lab and other groups, GCgx provides "a quick and easy way to query gene regulation of [glucocorticoids] in many human and mouse cell types. The GCgx team seems ready to improve the tool further with feedback and data contributions from users."

Franco came up with the idea for GCgx in early 2020, when much of NIH's bench research suddenly came to a halt due to the COVID-19 pandemic. He wanted to come up with a project that could be done outside of the lab and that could be accomplished using available data. **Qilin Cao**, postbaccalaureate fellow and the lead author of the aforementioned paper, took the idea and developed the web application.

"I think this is an example of how NIH postbacs can really make lasting contributions to their field of work," said Franco.

Franco hopes that a better understanding of how glucocorticoids work will enable scientists to develop effective treatments with fewer side effects. GCgx is free, secure, and available to intramural researchers as well as those outside of the NIH. For more information on how to use GCgx, go to https://gcgx.niaid.nih.gov. ●

Satabdi Nandi, a postdoctoral fellow in the Laboratory of Molecular Biology and Immunology in the National Institute on Aging, is investigating the generation of antibody diversity in mouse B cells.

Former NIH Director Francis Collins Named Temporary Science Advisor to the President

CREDIT FOR BOTH: CHIA-CHI "CHARLIE" CHANG, NIH

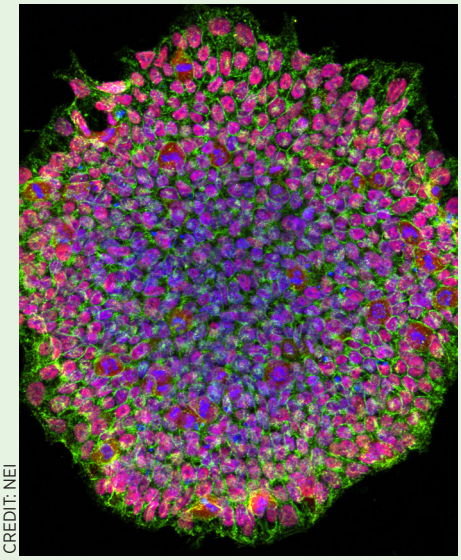
Former NIH Director Francis Collins (left) was recently named temporary science advisor to President Joe Biden. In December 2021, when Biden visited the NIH Bethesda campus, he and Collins greeted each other with a fist bump.

On February 16, 2022, President Joe Biden announced that **Francis Collins** and Alondra Nelson would temporarily replace U.S. Science Advisor Eric Lander, who resigned on February 7, 2022, after a White House investigation determined that he had violated the administration's Safe and Respectful Workforce policy. Lander was the director of the Office of Science and Technology (OSTP), the science advisor to the president, and a co-chair of the President's Council of Advisors on Science and Technology (PCAST).

Collins, who retired as NIH director in December 2021, will temporarily perform the duties of science advisor to the president and be a co-chair of PCAST. Nelson, who is OSTP's deputy director for science and society, will temporarily perform the duties of the OSTP director. They will serve in these roles until permanent leadership is nominated and confirmed.

"In the selections of Dr. Alondra Nelson and Dr. Francis Collins, President Biden has doubled down on science," according to a White House Briefing statement. "The selections are responsive to the dual importance of a strong OSTP that can drive science and technology solutions to our greatest challenges—and the very specific attention the President wants to give to the creation of a new ARPA-H [Advanced Research Projects Agency for Health] research and discovery agency, the building of support for a Cancer Moonshot, the search for a new head of NIH, and the broad advisory work of PCAST." ●

Intramural Research Briefs



CREDIT: NEI

NEI et al.: A human induced pluripotent stem-cell colony from a patient with an eye disease called OCA. The image was acquired using a confocal microscope and is stained for pluripotency marker proteins. The red color depicts transcription factor OCT4, green is SSEA4 protein, and blue represents the nucleus of the cells.

NEI, NCATS, NHGRI: RESEARCHERS DEVELOP FIRST STEM-CELL MODEL OF EYE DISEASE

NEI researchers have developed the first stem-cell model for oculocutaneous albinism (OCA), a set of genetic conditions that adversely affect pigmentation in the eye, skin, and hair. The disease-in-a-dish model will be used to further study this condition and to test new drug candidates.

People with OCA lack pigment in their retinal pigment epithelium (RPE), which supports the function of important light-sensing regions of the eye. This can result in a malformed optic nerve and an underdeveloped fovea, the part of the retina responsible for high-acuity vision. There is no approved treatment for most forms of OCA, and it cannot be studied very well using animal models.

In this method, researchers collected skin cells from patients with OCA as well as from healthy volunteers. These cells were reprogrammed into induced pluripotent stem cells and then differentiated into RPE cells. The researchers were able to show that these cultured RPE cells exhibited the pigmentation defects of OCA in vitro, making them an effective model to study how lack of pigmentation affects RPE structure and function. According to the authors, these results represent a significant step toward developing novel treatments for OCA. (NIH authors: A. George, R. Sharma, T. Pfister, M. Asu-Abab, N. Hotaling, D. Bose, C. DeYoung, J. Chang, D.R. Adams, T. Cogliati, K. Bharti, and B.P. Brooks, *Stem Cell Rep* **17**:173–186, 2022)

[BY HENRY DIECKHAUS, NINDS]

NIDDK: DRUGS TARGETING SKELETAL MUSCLE METABOLISM MAY HELP TREAT DIABETES

Skeletal muscle (SKM) is responsible for more than 70% of the body's glucose consumption. Insulin resistance in this tissue can reduce removal of sugar from the blood and lead to type 2 diabetes (T2D). NIDDK researchers found that clenbuterol selectively targets SKM sugar metabolism and shows promise as a potential new treatment for people with T2D.

Clenbuterol is used to treat asthma and chronic obstructive pulmonary disease. It stimulates the beta-2 adrenergic receptor (B2-AR) commonly found on cell membranes. In this study, the drug was fed to mice that were specially treated to induce a state of insulin resistance and elevated blood glucose, as seen in T2D. The researchers found that clenbuterol lowered blood glucose concentrations and improved whole-body glucose homeostasis despite having no effect on insulin sensitivity—a result that suggests stimulating B2-AR on the SKM membrane activates a pathway that enhances glucose metabolism. When the drug was tested on genetically modified mice that lacked SKM B2-AR, they did not show improved glucose tolerance with clenbuterol treatment. (NIH authors: J. Meister, D.B.J. Bone, L.F. Barella, R.J. Lee, A.H. Cohen, O. Gavrilova, Y. Cui, M. Chen, L.S. Weinstein, and Jürgen Wess, *Nat Comm* **13**:article 22, 2022)

[BY JONATHAN CHU, NIAID]

NCI: PERSONALIZED IMMUNOTHERAPY A POTENTIAL TREATMENT FOR METASTATIC BREAST CANCER

Researchers at NCI have discovered a potential new avenue to treat people with hormone receptor–positive metastatic breast cancer (mBrCa), traditionally thought of as an often-incurable stage of disease with limited response to current immunotherapies.

The results of an ongoing phase 2 clinical trial now show that using a type of immune cell called tumor-infiltrating lymphocytes (TILs), which are produced by some patients, can lead to substantial mBrCa tumor regression. TILs fight cancer by recognizing a fragment of a protein on the tumor's surface produced by specific mutations in the tumor's DNA. The study team used whole-genome sequencing to identify these mutations in tumor samples from 42 women with mBrCa and found that 28 of the women had TIL's that recognized their tumor.

For six of these women, the researchers grew large numbers of their mutation-specific TILs in a lab and then returned them to each patient by intravenous infusion. Three showed substantial tumor regression. These findings show the promise of personalized immunotherapy as a treatment for mBrCa and call for further studies to determine whether it can maintain a robust and durable antitumor response. (NIH authors: N. Zacharakis, L.M. Huq, S.J. Seitter, S.P. Kim, J.J. Gartner, S. Sindiri, V.K. Hill, Y.F. Li, B.C. Paria, S. Ray, B. Gasmi, C. Lee, T.D. Prickett, M.R. Parkhurst, P.F. Robbins, M.M. Langhan, T.E. Shelton, A.Y. Parikh, S.T. Levi, J.M. Hernandez, C.D. Hoang, R.M. Sherry, J.C. Yang, S.A. Feldman, S.L. Goff, and S.A. Rosenberg, *J Clin Oncol* 2022; DOI:10.1200/JCO.21.02170)

[BY LARISA GEARHART-SERNA, NCI]

NIDA: SUICIDES BY DRUG OVERDOSE INCREASE IN SOME GROUPS DESPITE OVERALL DECLINE

A recent NIDA-led study published in the *American Journal of Psychiatry* found that intentional drug-overdose deaths saw an overall decline in recent years in the United States, but increased for certain groups. The investigators discovered that suicide rates by drug overdose increased in younger men and women (ages 15–24), elderly men and women (ages 75–84), and non-Hispanic Black women of all ages.

The research team analyzed data from between 2001 and 2019 from the Centers for Disease Control and Prevention's National Vital Statistics System and focused on data related to overdose deaths that were classified as intentional.

Moreover, the investigators found that women were more likely to die from intentional drug overdose than men, and specifically, women ages 45–64 had the highest rates of suicide by drug overdose. They also discovered that intentional drug overdose deaths occurred more in spring and summer months and were lowest during December. And more people died by intentional drug overdose on Mondays than on other days of the week.

"This research underscores the importance of external support structures and environmental factors in determining a person's suicide risk," said co-author **Emily Einstein**. (NIH authors: B. Han, W.M. Compton, E.B. Einstein, J. Cotto, J.A. Hobin, J.B. Stein, and N.D. Volkow, *Am J Psychiatry* **179**:163–165, 2022)

[BY SUNITA CHOPRA, NCI]

NHGRI, NIAMS: NEW SPECIES OF MICROBES DISCOVERED ON HUMAN SKIN

The human skin is the physical barrier to foreign pathogens and plays a crucial role in maintaining an ideal microbial diversity. Shifts in this diversity are often associated with skin diseases such as acne or atopic dermatitis. NIH scientists and their colleagues recently catalogued these microbes in a massive collaborative study. The new catalog, called the Skin Microbial Genome Collection, was recently published in *Nature Microbiology* and successfully identifies almost 85% of the microorganisms present in a skin sample.

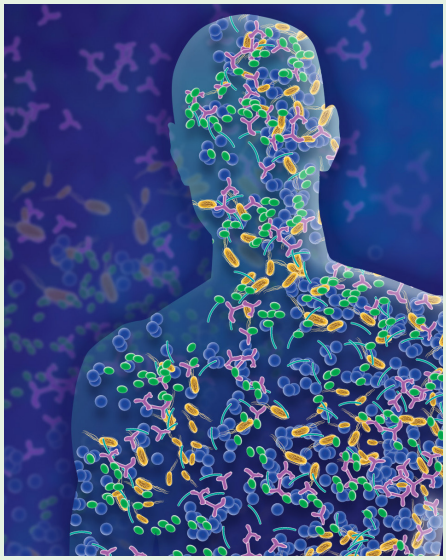
Newly identified were 174 bacterial species, 12 bacterial genera, and 20 jumbo phages, which are large viruses that infect bacteria. Researchers analyzed data from skin-swab samples and previously sequenced microbial samples taken from different body sites on 12 individuals. The authors used microbial culturing methods and genomic sequencing to make the new discoveries, which represent a 26% increase in the knowledge of skin bacterial diversity.

"The resource we've created will support research that explores skin health and seeks to understand the cause of these disorders," said **Julie Segre**, head of the Microbial Genomics Section at NHGRI. (NIH authors: S.S. Kashaf, D.M. Proctor, C. Deming, M.E. Taylor, H.H. Kong, and J.A. Segre, *Nat Microbiol* **7**:169–179, 2022; DOI:10.1038/s41564-021-01011-w)

[BY SATABDI NANDI, NIA]

NIDDK, NCI: BRAIN INFLUENCES INSULIN PRODUCTION

A new NIH study is the first to show clear evidence of a brain-to–beta cell circuit that regulates insulin secretion in mammals. Led by NIDDK scientists, the study identified a neuronal circuit in mice that connects the brain to the beta cells of the pancreas, the cells that produce insulin. The researchers found that the circuit originates from a small set of neurons in the paraventricular nucleus of the hypothalamus, which communicate with the pancreatic beta cells to control insulin production and monitor blood glucose levels in the body.



CREDIT: NHGRI

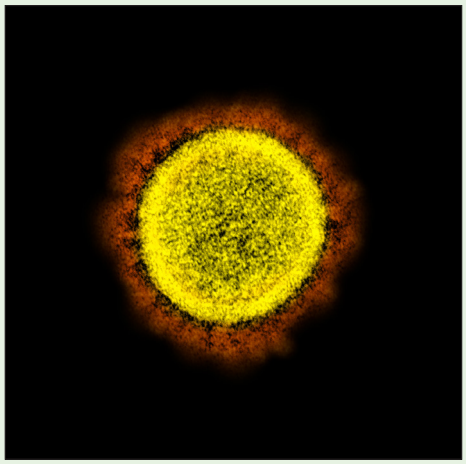
NHGRI, NIAMS: The microbiome is comprised of microorganisms that live in and on us and contribute to human health and disease. NIH researchers discovered new species of microbes that live on human skin.

When blood glucose became low, the neurons activated and communicated to the beta cells to stop producing insulin, preventing glucose concentrations from falling any further. Conversely, when the neurons were silenced, insulin release increased, and blood glucose dropped. The findings, which were published in *Cell Metabolism*, suggest that the brain elicits such protective mechanisms to overcome extreme and uncontrolled hypoglycemia. The authors propose that further research identifying similar neural circuits will advance understanding of the brain's role in regulating blood glucose and its impact on physiology and disease. (NIH authors: I. Papazoglou, J. Lee, Z. Cui, C. Li, G. Fulgenzi, Y.J. Bahn, R.A. Piñol, M.J. Krashes, and S.G. Rane, *Cell Metab* **34**:285–298, 2022) ●

[BY: LISA YUAN, NIDDK]

Read longer versions of these briefs at: https://irp.nih.gov/catalyst/v30i2/research-briefs.

COVID-19 Timeline at NIH (January–February 2022)



CREDIT: NIAID

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

January 1: The NIH Clinical Center implements changes to hospital operations due to significant increases in community COVID-19 cases. Urgent admissions and procedures will be prioritized, and less urgent procedures will be deferred or rescheduled to a later time.

January 3: NIH adopts the updated CDC guidance issued on December 27 for shortened isolation and quarantine periods for employees testing positive for or exposed to COVID-19. NIH now requires the ASTM Level 3 mask when working on-site.

January 4: Travel restrictions imposed again.

January 4: The "NIH Director's Blog" features *Science's* biomedical breakthroughs of 2021 that NIH played some role in advancing: artificial antibody therapies and antiviral pills to treat COVID-19; artificial intelligence approaches that predict structural changes in spike proteins of SARS-CoV-2 variants.

January 6: An NIH-funded study found that women receiving one dose of a COVID-19 vaccine during a menstrual cycle had an increase in cycle length of nearly one day. (*Obstet Gynecol* Jan 5, 2022)

January 7: NIH's Division of Occupational Health and Safety clarifies mask guidance issued on January 3: ASTM Level 3 masks are only mandated for staff in health care settings, staff returning after a positive COVID test or exposure, and everyone entering the Clinical Center, where masks will be provided upon entry. Staff who work in certain patient care and laboratory functions with potential high-risk COVID-19 exposures are already required to use N-95 or higher-level respirators.

January 7: In his email to staff, NIH Acting Director **Lawrence Tabak** reports that NIH COVID-19 testing services will now be reserved only for staff who are required to or have been approved to work on-site.

January 14: The CDC clarifies that surgical masks and respirators such as N-95s and KN-95s offer better protection from SARS CoV-2 compared with cloth masks.

January 18: All non-patient visitors arriving at an NIH facility are required to attest to their vaccination status. Starting January 24, those not fully vaccinated must provide proof of a negative COVID-19 test result within the past 72 hours to gain access to an NIH facility.

January 18: An NICHD-led study finds that SARS-CoV-2 infection during pregnancy may cause inflammatory immune responses in the fetus. (*Nat Comm* **13:**article 320, 2022)

January 18: On the "NIH Director's Blog," Acting NIH Director **Lawrence Tabak**, who also runs a lab at the National Institute of Dental and Craniofacial Research (NIDCR), reports on a collaboration with **Kelly Ten Hagen** (NIDCR) that demonstrated how O-glycosylation can influence SARS-CoV-2 and its ability to fuse to cells. The alpha and delta variants carry a spike mutation that could mean decreased O-glycosylation (*Proc Natl Acad Sci U S A* **118:**e2109905118, 2021).

January 20: COVID-19 vaccination does not affect the chances of conceiving a child, according to an NIH-funded study. (*Am J Epidemiol* kwac011, 2022)

January 20: A *Science* viewpoint essay, co-authored by NINDS Clinical Director **Avindra Nath**, highlights what is known about the effects of SARS-CoV-2 on the brain, the importance of more research into the causes of long COVID, and ways to treat its symptoms. (*Science* **375:**267–269, 2022)

January 21: NIH encourages all contractors with a PIV card to upload proof of COVID-19 vaccination by February 15. Contractors who elect not to do so will be required to follow non-patient visitors procedures (see January 18).

January 21: The Office of Intramural Training and Education urges trainees appointed using contract mechanisms to upload their proof of COVID-19 vaccination by January 31.

January 21: In his email to staff, NIH Acting Director **Lawrence Tabak** reports that the omicron surge is on a downward trend nationally; mentions the national court decision issued today that places a temporary hold on the implementation of the federal employee vaccine mandate; and shares updated mask recommendations that staff working at an NIH facility wear well-fitting, disposable surgical masks. Cloth masks alone are not allowed.

January 24: An NIH-funded study finds that social connectedness, sleep, and physical activity were associated with better mental health among youth during the pandemic. (*J Adolesc Health* **70:**387–395, 2022)

January 26: A clinical trial sponsored by NIH finds that in adults who had previously received a full regimen of any of the three COVID-19 vaccines currently authorized by the FDA, an additional booster dose of any was safe and prompted an immune response. (*New Engl J Med* 2022; DOI:10.1056/NEJMoa2116414)

January 26: A computer analysis of existing genomic data uploaded by NIH to a global sequence database uncovers 100,000 novel viruses, including nine new types of coronaviruses similar to SARS-CoV-2. (*Nature* **602:**142–147, 2022)

January 27: Acting NIH Director **Lawrence Tabak** hosts the ninth virtual Town Hall with over 10,000 attending online. NIH leaders answer questions and provide an update on the Office of the Director leadership transition, the current state of the pandemic, and changes

to travel, services, and return-to-the-physical-workplace plans due to surges in COVID-19 cases. Videocast (HHS only) at https://videocast.nih.gov/watch=44500.

January 27: The guidance issued on January 21 related to NIH contractor access to NIH facilities and properties based on vaccination status is paused as a result of the preliminary nationwide court injunction.

January 27: An NIAID-supported trial finds that the combination of remdesivir and a concentrated solution of antibodies that neutralize SARS-CoV-2 is not more effective than remdesivir for treating adults hospitalized with COVID-19. (*Lancet* **399**:530–540, 2022)

January 28: HHS Secretary Xavier Becerra emails all staff announcing a new video from the We Can Do This Campaign about the importance of getting a COVID-19 booster shot.

January 31: NIH permits non-mission-critical travel to resume.

January 31: An NIAID-supported study will assess whether temporarily reducing immunosuppressive medication taken during the days before and after an additional dose of an mRNA COVID-19 vaccine safely allows for better antibody response to vaccination in kidney- and liver-transplant recipients.

February 1: The "NIH Director's Blog" features a promising study demonstrating how a specially engineered protein particle can neutralize multiple SARS-CoV-2 variants in a mouse model. (*Nat Chem Biol* 2022; DOI:10.1038/s41589-021-00965-6)

February 2: NIAID announces a new pandemic preparedness plan targeting known viruses and identifying viral threats before they emerge.

February 3: NIH begins the voluntary At-Home Antigen Testing Pilot Program. Eligible staff who are reporting on-site at an NIH facility may receive at least an eight-week supply of rapid COVID-19 test kits at no cost.

February 4: In his weekly email to staff, NIH Acting Director **Lawrence Tabak** highlights guidance and new research from NIAID and their new pandemic preparedness plan.

February 7: An NICHD-funded study finds that pregnant women with moderate to severe COVID-19 infection appear to be at greater risk for common pregnancy complications than uninfected women. Mild or asymptomatic infection was not associated with increased pregnancy risks. (*JAMA* **327**:748–759, 2022)

February 9: HHS Deputy Secretary Andrea Palm emails staff to announce the next phase of the return-to-the-workplace process. Phase 2B employees will return beginning March 27, 2022, and Phase 2C employees will return beginning April 10, 2022.

February 9: In an email to all staff, NIH Acting Director **Lawrence Tabak** writes that he expects the return to on-site work process will be gradual and that NIH leadership is exploring the use of continued workplace flexibilities.

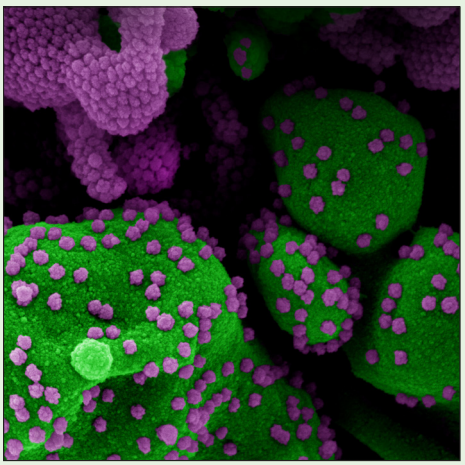
February 11: NIH resumes normal COVID-19 reporting procedures for positive COVID-19 test results, which had been temporarily suspended for people working off-site during the omicron surge.

February 14: NIH increases the allowable density for primary facilities around the country: Maryland locations will be allowed one person per 35 square feet (in July 2020, it was 1 person per 125 square feet).

February 15: NIH launches a COVID-19 facts campaign on social media under the tag #NIHCOVIDFacts to educate and dispel common COVID-19 myths and highlight NIH's role in the pandemic.

February 16: President Joseph Biden announces that former NIH Director **Francis Collins** will temporarily perform the duties of science advisor to the President and co-chair of the President's Council of Advisors on Science and Technology.

February 17: An NHLBI-led study identifies types of autoantibodies, which target a person's own organs and systems, that correlate with severe COVID-19 illness and may help explain mechanisms associated with severe blood clotting. (*Arthritis Rheumatol* 2022; DOI:https://doi.org/10.1002/art.42094)



CREDIT: NIAID

Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-COV-2 virus particles (purple), isolated from a patient sample. Image from NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

February 18: NIH Acting Director **Lawrence Tabak** emails all staff to remind them that NIH mask requirements remain in place, even as county and state mask mandates are lifted.

February 22: The NIH Clinical Center resumes walk-in appointments for asymptomatic COVID-19 testing services for staff working on-site at an NIH facility, which had been paused during the omicron surge.

February 23: HHS Assistant Secretary for Administration Cheryl Campbell emails staff to announce a new COVID-19 screening testing program for employees who are not fully vaccinated and must work on site.

February 24: A study led by NIMHD finds that people from all major racial and ethnic minority population groups and marginalized groups in the United States report experiencing more COVID-19–related discrimination than white adults. (*Am J Public Health* **112**:453–466, 2022; DOI:10.2105/AJPH.2021.306594) ●

Read a more detailed version of this timeline, complete with links, at https://irp.nih.gov/catalyst/v30i2/covid-19-timeline-at-nih-january-february-2022.

Meet the Makers

CONTINUED FROM PAGE 1

such as physics and chemistry to solve biomedical problems. And by joining forces with researchers across NIH's intramural research program (IRP), they're moving discovery into entirely new places.

Team science creates new technology

In December 2019, **Kaitlyn Sadtler** arrived at NIH and was handed the keys to her lab. As a Stadtman Investigator and head of NIBIB's Section on Immunoengineering, she was eager to delve into how the body's immune response might enhance tissue regeneration. But the COVID-19 pandemic in early 2020 soon prompted an abrupt change of course: Her lab quickly refocused, launching a nationwide SARS-CoV-2 survey with the goal of determining the proportion of people with undiagnosed COVID-19 infections to understand how the virus was spreading.

First, they needed new tests. Over 10,000 study volunteers would eventually mail at-home blood collection kits back to Sadtler's lab to be tested for the presence of SARS-CoV-2 antibodies, which would indicate a previous infection.

In March 2020, Sadtler's lab led a cross-institute project to develop enzyme-linked immunosorbent assays (ELISAs) that could detect SARS-CoV-2 antibodies. **Dominic Esposito's** Protein Expression Laboratory at the National Cancer Institute (NCI) generated viral proteins that would be essential reagents for the new assays. Broad data-collection efforts were enhanced by capabilities at the National Center for Advancing Translational Sciences. Combined with expertise from researchers at the National Institute of Allergy and Infectious Diseases, a new set of ELISAs were born. Their protocol was published in Nature Communications (*Nat Commun* **12:**article number 113, 2021).

"We now have a panel of 12 ELISAs to look at antibody reactivity against different proteins in the SARS-CoV-2 virus as well as different variants," said Sadtler.

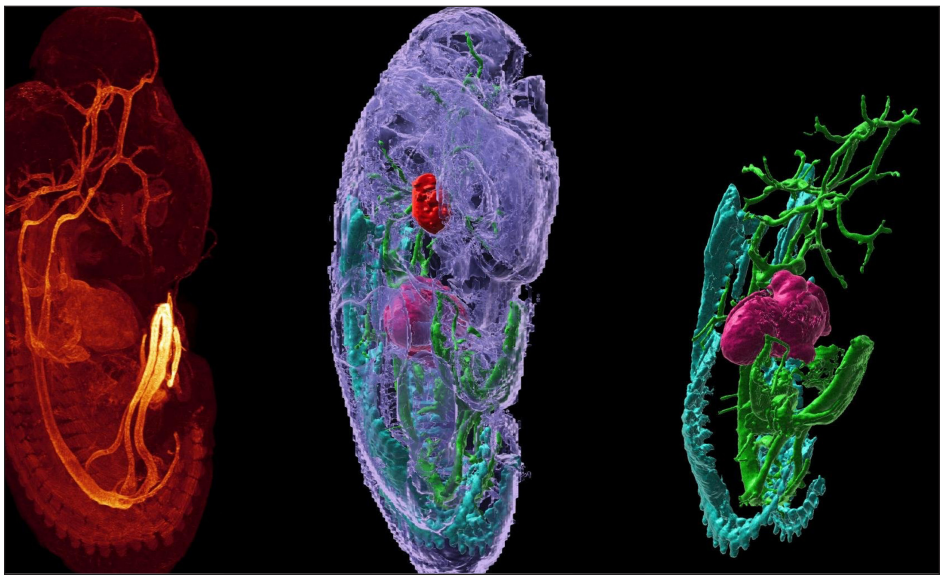
Finding collaborators

How do investigators with common goals find each other? Often it's word of mouth, but another way is through scientific interest groups (SIGs). Sadtler helped establish the COVID-19 SIG in 2020 and recently formed the new Biomedical Engineering SIG with fellow bioengineer **Matthew Wolf**, a Stadtman Investigator at NCI. The latter SIG aims "to integrate the bioengineering community across different ICs," Sadtler said.

Partnerships outside of NIH—sometimes just across the street—often spark innovation. Sadtler's immunoengineering lab has resumed its work on regenerative medicine, and one project is with colleagues at Walter Reed National Military Medical Center (Bethesda, Maryland), who are testing a drug to prevent scar tissue from forming in injured rat muscle. The NIBIB team characterizes the immune response to the injury and correlates that with changes in muscle physiology found by the Walter Reed investigators.

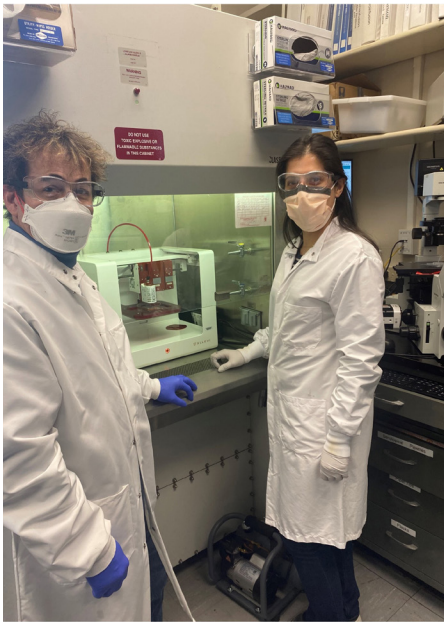
Further work at Sadtler's lab focuses on how a natural biologic scaffolding known as decellularized extracellular matrix (dECM) can be used to orchestrate a productive immune response to injury and regenerate tissue. She's discovered that biomaterials like dECM attract critical immune players such as helper T cells, which then cue stem cells to produce healthy tissue instead of scar tissue. Such technology has shown promise in a variety of clinical settings from wound healing to regenerating damaged muscle and cartilage and might one day be used to regrow entire human organs.

Sadtler has even had conversations with physicians who wonder whether it's possible to develop ways for surgical wounds to heal faster. "Being a bioengineer is fun," she said. "We get to bridge that gap between basic studies and talking to a surgeon and asking: 'What would you actually use if I designed something?'"



M. LINDHURST, S. WINCOVITCH (NHGRI); Y. SU, H. VISHWASRAO (NIBIB)

The Advanced Imaging and Microscopy Resource offers cutting-edge prototype microscopes paired with high-performance computing that can improve image quality and recording speed. Shown: A mouse embryo's fluorescently labeled smooth muscle actin and autofluorescence were imaged using a multi-view light sheet microscope, which rapidly acquires two views of a sample that can be computationally fused into a single high-resolution 3D rendering.



CREDIT: NICOLE MORGAN, NIBIB

Robert Fischer (NHLBI) uses some of the advanced imaging tools offered by NIBIB to study the inner workings of cells at ultra-high resolution. Here, Fischer (left) and **Paniz Rezvan Sangsari** (NIBIB) use an Allevi extrusion bioprinter to make artificial vessels.

AIMing for a closer look

NIBIB's **Hari Shroff** runs the Advanced Imaging and Microscopy Resource (AIM) in Building 13. A resource for all intramural scientists, this trans-NIH facility offers cutting-edge prototype microscopes paired with high-performance computing that can improve image quality and recording speed. And new systems capable of witnessing the birth of a neuron or marveling at mitochondria in high-resolution are in the works. "I consider myself a tool developer, and I want people to use my tools," said Shroff, who also leads the Laboratory of High Resolution Optical Imaging (HROI), located just next door to AIM. HROI has been an incubator for instruments now deployed at core facilities throughout campus, including a light sheet microscope and a high-speed super-resolution microscope that were patented by NIH and now produced commercially.

Shroff often reaches out to IRP investigators to see what cells and tissues they have that could highlight a new instrument's capabilities. His group recently published a paper (*Nature* **600:**279–284, 2021) in which they described how their new triple-view line-scanning confocal microscope captured extraordinary super-resolution images. Some of the imaged samples, such as mouse esophagus tissue and proteins interacting within immune cells, were specially prepared by colleagues at NCI and the National Heart, Lung, and Blood Institute (NHLBI).

Robert Fischer at NHLBI studies cell biology in 3D by preparing live cells in collagen gels. He tested HROI's prototype structured illumination microscope to reveal the inner workings of cells at twice the resolution of conventional microscopes, which is approximately 250 nanometers. The technique rapidly scans a sample, and then machine-learning algorithms fuse together 3D images. While the method is useful for capturing live cellular processes (such as a quickly moving virus), it can distort images in the third dimension, so the HROI team has been improving the optics and algorithms. "Those images now appear [in focus from all directions] with 100-nanometer-scale resolution," said Shroff. "I think there's a lot of biology that lives at that scale."

The bioengineering landscape is rife with instances of ingenuity in which existing technology is modified or used in unexpected ways. Consider adaptive optics: Light distortion entering a lens is measured in real-time and compensated for by a deformable mirror, which corrects the aberration. Astronomers have used the technology for decades in ground-based telescopes to scan the heavens, but in recent years, the technique has been adapted to look within the body. Stadtman Investigator **Johnny Tam** leads a National Eye Institute (NEI) team that is using a custom-built adaptive optics scanning light ophthalmoscope at the NIH Clinical Center (CC). This instrument enables the team to noninvasively image the retinal cells of people with diseases such as age-related macular degeneration. Back at Shroff's lab, researchers are integrating adaptive optics into microscopy. They hope it will sharpen blurry images caused by scattered light that occurs over the curved surface of thicker samples.

How to efficiently analyze tomes of data is a challenge that scientists are grappling with. One of Shroff's prototype light sheet microscopes looks at cleared tissue (tissue made transparent by using solvents). This microscope can collect terabytes of data, say, on an entire mouse brain, in a day. Investigators can then spend months searching for just the key pieces relevant to their work. A biologist sifting through volumes of data on that mouse brain might be tracing a single axon and only be interested in the few instances where it synapses. This is an area that Shroff hopes advances in artificial intelligence can help speed up the search process. "We need biologists to road test our tools currently in development," said Shroff. They can "highlight the problems…so we know what the next generations of tools should do."

Meeting technical support needs

Searching for a rheometer on campus? Look no further than the Trans-NIH Shared Resource on Biomedical Engineering and Physical Science (BEPS). Don't know how to use a rheometer? BEPS can help with that as well. BEPS's five units can support any NIH scientist in a range of applications whether it's engineering custom immunoassays and microdevices or providing training on specialized instruments and laboratory techniques.

"We try to be at the leading edge of

CONTINUED ON PAGE 14

Meet the Makers

CONTINUED FROM PAGE 13

CREDIT: CARLO PIERPAOLI, NIBIB

In NIBIB's Laboratory on Quantitative Medical Imaging (QMI), **Carlo Pierpaoli** is a pioneer in the field of diffusion magnetic resonance imaging (dMRI), which uses specific MRI sequences and software to visualize the size and microstructure of white matter in the brain. The technique is being used to gain insight into healthy brains as well as the brains of people who've had a stroke or who have neurodegenerative disorders such as Alzheimer disease. Shown: QMI staff scientist **Okan Irfanoglu** performing an MRI scan of a research subject.

what people need," said BEPS Acting Chief **Nicole Morgan**. She's currently working with **Clare Waterman** at NHLBI to understand how forces generated by circulating blood in straight and curved vessels affect the structure of cells lining the vessels' walls. They're using a newly purchased extrusion bioprinter to build model blood vessels and are able to quantify the model's elasticity and stiffness with a rheometer—an important step to ensuring an appropriate environment for cell growth. Understanding such dynamics could yield insights into how immune or cancer cells move throughout the body.

"A lot of the things that we work on are heavily customized and optimized for specific research problems," said Morgan, who also heads the Microfabrication and Microfluidics Unit. Her team can quickly create multiple versions of a device to arrive at the one that best fits a project.

Morgan's lab recently fabricated a device that mimics the branching microvasculature network found in the lung. Researchers at the National Institute of Arthritis and Musculoskeletal and Skin Diseases who investigate autoimmune diseases used it to compare how healthy and diseased neutrophils might navigate through pulmonary capillaries.

Moving to BEPS's Micro Analytical Immunochemistry Unit, run by **Heather Kalish**, are the SARS-CoV-2 assays and automated ELISA equipment that have already been used in other IRP projects. Kalish's team also hosts a new matrix-assisted laser desorption/ionization–time of flight mass spectrometry system, a powerful tool that can generate heat maps of proteins and other organic molecules in tissue sections. The unit also operates the only inductively-coupled-plasma optical emission spectrometry system on campus, to analyze trace metals in biological samples.

BEPS's three other units—the Electron Microscopy Unit, the Quantitative Methods for Macromolecular Interactions Unit, and the Scanning Probe Microscopy Unit—support a myriad of other IRP projects, too.

Novel instrumentation and design

If you've needed assistance testing the auditory function of rodents or endeavored to build a handheld hematoma detector, you may have worked with **Tom Pohida's** group of electrical, biomedical, computer, and mechanical engineers. He's chief of the Instrumentation Development and Engineering Application Solutions (IDEAS) Section, the third and newest trans-NIH shared resource hosted at NIBIB. Formerly under the Center for Information Technology, Pohida's lab will continue to focus on integrated instrumentation.

"IDEAS cuts across clinical and basic sciences," said NIBIB Scientific Director **Richard Leapman**. It "can work with individual PIs in areas including tissue engineering, bioreactors, sensors, electronic components, and 3D-printed clinical devices such as those used in the [NIH Clinical Center]."

Leapman also highlights another of NIBIB's team science components, the Positron-Emission Tomography Radiochemistry and Imaging Core, led by **Dale Kiesewetter**. This facility innovates new ways to create biomarkers known as probes, which are used to noninvasively visualize cellular processes in medical diagnostic imaging. In collaboration with other NIH scientists, the group has already developed probes to study biological events from inflammation and cellular metabolism, to cancer metastasis and the growth of new blood vessels.

Improving methodology

"We are not just providing technical support, we're working in partnership with [clinicians] to develop new methods," said **Carlo Pierpaoli**, head of NIBIB's Laboratory on Quantitative Medical Imaging (QMI). Pierpaoli is a pioneer in the field of diffusion magnetic resonance imaging (dMRI), which allows researchers to visualize the size and microstructure of white matter in the brain. The technique is being used to gain insight into healthy brains as well as the brains of people who've had a stroke or who have neurodegenerative disorders such as Alzheimer disease. (*Magn Reson Med* **85:**2696–2708, 2021).

As they continue to refine their craft, the QMI lab created a software suite called TORTOISE that makes their methodologic improvements available to any researcher and is currently being used at other neuroscience centers to analyze dMRI data.

QMI's techniques are being used clinically, too. QMI scientists collaborated with investigators from the National Human Genome Research Institute, NEI, and the CC to phenotype patients with genetic facial weakness disorders such as Moebius syndrome. (*Brain Commun* **2:**issue 1, 2020; DOI:10.1093/braincomms/fcaa014)

Pierpaoli is also working with a European group that uses focused ultrasound to treat essential tremor, a debilitating condition resulting in uncontrolled limb movement, making basic tasks such as eating nearly impossible. The FDA-approved treatment uses ultrasound to heat and destroy the small patch of brain tissue responsible for the tremor. But the surgical planning is imprecise. Clinicians currently use anatomical landmarks and lower-intensity ultrasound to localize where the final treatment should be, which could accidentally damage some healthy brain tissue. The dMRI methods could minimize that risk by creating an accurate map of the brain to more precisely determine where the ultrasound should be directed. Pierpaoli has already seen his technology used successfully.

He advocates for getting out of the lab to see what questions others are asking. He has lectured at international clinical conferences and presented at the CC's grand rounds. "You need to stick your neck out of your own lab and listen to the clinicians, it is important to become aware of unmet needs that you may be able to address," he said.

Accelerating bioengineering at NIH

A thread of bioengineering weaves throughout NIH. "There's just not enough of it," said NIBIB Director **Bruce Tromberg**. "But the demand is extremely high."

Enter the NIH Center for Biomedical Engineering and Technology Acceleration (BETA), Tromberg's bold vision for a centralized entity that will unite multidisciplinary teams of technology developers on campus. BETA will provide the people, culture, and tools to propel technology-driven interdisciplinary research, training opportunities, and clinical translation at NIH.

The new center will draw from existing NIBIB core facilities and resources. Spaces in Building 13, the Porter Neuroscience Research Center (Building 35), and the CC have been identified as places that will accommodate a growing team of innovators and state-of-the-art equipment. As it evolves, Tromberg hopes that BETA will facilitate joint appointments within the IRP, attract biomedical engineers from outside of NIH, and have the potential to form industry partnerships and commercialize new technology. BETA could facilitate the enhancement of synthetic biology and new biomaterials, artificial intelligence, and wearable sensors paired with digital health platforms that help patients self-manage their conditions. The groundwork for research programs is being laid now and a BETA director is expected to be appointed by this summer.

Tromberg points to the enormous growth of the country's more than 140 biomedical engineering departments—many combining engineering and medical schools—that have become centers of innovation and retain energy and talent through an entrepreneurial startup ecosystem. He envisions the same happening at NIH. "That would be a great outcome, and a logical one."

CREDIT: CHIA-CHI "CHARLIE" CHANG, NIH

NIBIB Director **Bruce Tromberg** is planning an NIH Center for Biomedical Engineering and Technology Acceleration, a centralized entity that will unite multidisciplinary teams of technology developers on campus and facilitate the enhancement of synthetic biology and new biomaterials, artificial intelligence, and wearable sensors paired with digital health platforms that help patients self-manage their conditions.

Bioengineers are a practical bunch, united in their ambition to bring new technologies from an idea to a tool that contributes meaningfully to human health. And according to Tromberg, the possibilities are limitless. "Technology itself is never done," he said. "There are always ways to continue to push the envelope." ●

To learn more about how NIBIB can help you with your projects, go to https://www.nibib.nih.gov/labs-at-nibib.

To collaborate with NIBIB's shared resources, email them directly at:

- AIM: hari.shroff@nih.gov
- BEPS: morgann@mail.nih.gov
- IDEAS: IDEAS-info@mail.nih.gov

Itching for Answers

CONTINUED FROM PAGE 1

Investigator and immunologist **Wanjun Chen** recently set out to determine how itch arises during wound healing. For most of us, itch is a temporary symptom that emerges as a scratch or scrape heals. But for large or severe wounds, including burns, itching can be agonizing and persistent.

Chen and then-postdoc **Junji Xu** found high amounts of a cytokine called interleukin-31 (IL-31) in skin wound tissue from mice at the peak of itch responses. In addition, wound-induced itching was eliminated in genetically engineered mice that lacked IL-31. Further experiments showed that IL-31 is released by immune cells called dendritic cells, which rush to sites of skin damage to defend against pathogens. The results pointed to an important role for IL-31 in wound-induced itching.

Although they had pinpointed the likely immune mechanisms, Chen's team needed to understand the other side of the equation—how that activity translates into the itchy feeling perceived by the brain.

"We knew the immunological part very well, but we're not experts in the neural mechanisms," said Chen. So his group turned to their NIDCR colleague **Mark Hoon**, a senior investigator and neuroscientist who's an expert in neurons that detect itch and pain.

With help from Hoon's lab, the scientists found that IL-31 elicits itching by stimulating itch-sensing nerves that relay signals from the wound site toward the brain (*Immunity* **53:**371–383.e5, 2020).

"There's value in venturing beyond our particular areas of expertise, because the molecular activities that occur in the skin don't recognize the borderline between immunology and neuroscience," said Hoon. "There's so much at the intersection of the fields that's really important to understand."

Further research will be needed to determine whether the IL-31 findings apply to humans. "Ultimately, the goal is to develop a therapy," said Chen. "But IL-31 may not be the only cytokine driving itch during wound healing—there may be others too."

CREDIT: NIDCR

Scientists in **Wanjun Chen's** lab found that the interleukin-31 cytokine elicits itch during wound healing. Shown (from left): Chen discussing projects with former fellows **Brittany Abbatiello** (postbac) and **Eric Tu** (postdoc).

Recent research from Hoon's group appears to align with this idea. "There's only a certain set of cytokines that are likely to be important for itch, and different combinations of cytokines may drive different itch-related conditions," he said.

Hoon's team looked at cytokines present in skin samples from people with chronic itch–related conditions such as psoriasis. For most, a cytokine called oncostatin M (OSM) predominated.

The researchers found that OSM enhanced the activity of itch-detecting neurons in a lab dish, and that injecting it into the skin of mice intensified scratching behaviors. In a mouse model of psoriasis-induced chronic itch, scratching was almost entirely eliminated by giving a drug that blocks OSM from interacting with itch neurons, pointing to OSM's importance in driving chronic itch (*Sci Transl Med* **13:**eabe3037, 2021).

"Small-molecule drugs that block OSM's activity could be promising therapies for chronic itch," Hoon said.

But not every patient may benefit from an OSM-blocking therapy. "On average, across all the patients we studied, there was very high production of OSM—but not in every individual," said Hoon. Instead, some skin samples had high concentrations of IL-31, the cytokine Chen's team found to be linked to wound itching. Further experiments by Hoon's group showed that IL-31's effects on itch neurons were similar to OSM's.

"A number of cytokines could produce these effects," Hoon said. "Ideally, if you want to treat a person most effectively, you would try to determine which molecules are elevated in their skin and target them."

With that goal in mind, the Hoon and Chen labs plan to continue identifying itch-related compounds and defining their roles, with the aim of painting a more complete picture of itch in its many forms. ●

Catherine Evans is a science writer in the National Institute of Dental and Craniofacial Research's Science Communication and Digital Outreach Branch.

How Community-Engaged Research Combats Health Disparities

Stephen B. Thomas Delivers the History of Medicine Lecture

BY JANETTE NORRINGTON, OD

"You know what we do? We serve the people first, we build the relationship first, we build the trust first, and then the research flows naturally," said Stephen B. Thomas, director of the Center for Health Equity at the University of Maryland School of Public Health (College Park, Maryland). In his History of Medicine talk at NIH last year, he spoke about how the United States Public Health Service Syphilis Study at Tuskegee (1932–1972)—in which Black men with syphilis were not treated even when penicillin treatment became widely available in 1943—has affected the trust and willingness of African Americans to participate in public health research. Then he offered a way forward.

The COVID-19 pandemic has brought health disparities to the forefront of public health in the United States. Many racial and ethnic minority groups, including African Americans and Hispanics, are at higher risk of getting sick and dying from the disease. Underrepresentation of these groups in clinical research and barriers to accessing health care perpetuate health inequity.

Thomas described how hyper-local community-engaged research can combat COVID-19 health disparities when health service systems, community-based organizations, and patient advocacy groups work collaboratively with underserved populations. Culturally tailored community-based interventions, ethical recruitment of minorities, and provision of services can increase the willingness of minority groups to participate in health research.

When Thomas came to the Maryland Center for Health Equity in 2010, he set out to develop innovative community-engagement initiatives to eliminate racial and ethnic health inequalities. He and a team of researchers developed the Health Advocates In-Reach and Research (HAIR) campaign, which provided an infrastructure to use salons and barbershops as trusted information centers for medical services in culturally tailored and effective ways.

"[We are] reaching within to train barbers and stylists so that the barbershops and salons could be places where our community learns about clinical trials," said Thomas. "So that the knowledge [about treatments and prevention] is not something [people] are learning about for the first time when they're in a hospital and being told that they have a cancer diagnosis." HAIR brought health professionals to underserved communities to educate and empower people and advance opportunities for clients to participate in clinical trials.

HAIR serves as the template for the Shots at the Shop campaign, a White House-endorsed national effort to increase COVID-19 vaccine uptake in minority communities through partnerships with barbershops and salons. The program trains hairstylists and barbers to dispel myths and disinformation about COVID-19 so their clients can make informed health decisions as well as provides clinicians and COVID-19 vaccines to the shops. Through this initiative, barbershops and salons in the Black community are now recognized as legitimate and safe places for engaging the population in health promotion and disease prevention. Thomas believes that the success of HAIR and Shots at the Shop can be scaled and expanded to other health services such as flu shots and diabetes screenings.

Thomas is building a team mentoring program to train the next generation of health-disparities and community-engaged researchers. Through the Center of Health Equity, he promotes supportive environments for early-career scholars to successfully conduct research while maintaining trust within the community.

Thomas' methods for doing research are gaining traction. In February 2022, the National Institute on Drug Abuse Intramural Research Program signed a formal collaboration agreement with his center that will promote health equity and improve community engagement through education, training, and evidence-based research activities. New programs to be developed by the partnership include working with underserved communities in the Baltimore and Washington, D.C., areas; enhancing research practices to be more inclusive and accessible toward developing personalized treatments for alcohol and substance-use disorders; and promoting increased diversity among future scientists in the field of addiction.

"This historic agreement is one of many silver linings of the pandemic," said Thomas. "It bends the biomedical research enterprise toward a more equitable distribution of scientific discoveries." ●

A videocast of Thomas' talk, "Reframing Lessons from the Syphilis Study Done at Tuskegee (1932—1972) to Address the COVID-19 Pandemic: From Vaccine Hesitancy to Vaccine Confidence," presented on October 7, 2021, is at https://videocast.nih.gov/watch=43897.

Janette Norrington, a postdoc in the Office of Intramural Training and Education, is interested in pursuing a career in science communication.

Lasker Clinical Research Scholars

FREDDY ESCORCIA, NINDS

SUCHITRA HOURIGAN, NIAID

ROBERT HUFNAGEL, NEI

MARIELLE YOHE, NCI-CCR

For more information on the Lasker Clinical Research Scholars Program, go to https://irp.nih.gov/careers/trans-nih-scientific-recruitments/lasker-clinical-research-scholars

The Lasker Clinical Research Scholars Program provides a select group of individuals early in their scientific careers with the funding and institutional support to start their own labs at NIH. After five to seven years of independent research in the intramural research program (IRP), the scholars are given the option to apply for three years of funding for work outside of NIH or to remain as investigators at NIH. Read about the four newest scholars.

FREDDY ESCORCIA, M.D., PH.D.

Center for Cancer Research, National Cancer Institute

Engineering Radioactive Molecules to Treat Cancer: A successful career in biomedical research was never a sure thing for **Freddy Escorcia**. Though he was born in Nicaragua to two physician parents, his family fled to Canada as political refugees when he was 7 years old, at which point his parents were required to retake their medical board exams and redo their medical residencies in order to continue practicing medicine. It was his father's residency program that initially brought him to the United States at the age of 12, but his school years did little to inspire scientific curiosity.

"Until I was an undergraduate student, science was largely presented as a complete work to be memorized," he explained. "I still recall a chemistry professor mentioning that a certain phenomenon was believed to be occurring through a particular mechanism, but her laboratory was studying this further to determine if this was, in fact, the case. That experience opened the possibility that I could contribute to the scientific canon, even in some small way."

His undergraduate degrees in bioengineering and chemistry now inform his efforts to create new ways to monitor and treat pancreatic and liver cancer. When he is not using his lab skills to brew home-made beer, Escorcia cooks up cutting-edge radionuclides, radiation-emitting molecules that bind selectively to tumors. The radiation not only kills cancer cells by damaging their DNA, but it can also be picked up by medical imaging techniques to enable physicians to see the sizes and locations of tumors. What's more, because the radionuclides can attach only to molecules on the surface of tumors, the cell-killing radiation they emit mostly spares healthy cells from harm, unlike many current radiation and chemotherapy treatments that cause significant side effects.

Of course, being on the leading edge of cancer medicine is not easy, but the environment in the IRP and the support of the Lasker Program give Escorcia the freedom to pursue this sort of high-risk-high-reward research.

SUCHITRA HOURIGAN, M.D.

National Institute of Allergy and Infectious Diseases

Manipulating the Microbiome to Prevent Disease: Cutting-edge research can sometimes involve testing procedures that might seem bizarre to most people. This strangeness is perhaps most true of research on the microorganisms living on and in our bodies, known as the microbiome, because this work sometimes involves having people ingest bacteria-filled pills or rubbing microbes on their skin.

As strange as such strategies might appear, **Suchitra Hourigan** believes they could play an important role in lowering people's risk for a wide array of conditions related to inflammation, including allergies and obesity. She is particularly interested in taking early action to influence babies' microbiomes.

"The microbiome develops rapidly in the first few years of life, and during this time it is essential in shaping immune system development," she explained. "This area particularly excites me because simple interventions very early in a child's life could have the possibility of improving their future health and preventing disease."

Prior to joining NIH, Hourigan was vice chair of research for the Inova Children's Hospital in Falls Church, Virginia, where she launched a randomized, controlled trial—the first of its kind—that tested how

exposing babies delivered via C-section to microbes found in their mothers' vaginas would affect their health during the first few years of their lives. C-sections are often necessary, but babies born this way are at increased risk for the inflammatory diseases Hourigan studies, possibly because the infants are not exposed to their mothers' vaginal microbiomes, which would otherwise make themselves a part of the baby's microbiome as well. If the approach Hourigan is testing improves health outcomes, it could provide a simple way to lower disease risk in the nearly one-third of babies in the United States born via C-section.

As one of NIH's newest Lasker Scholars, Hourigan will continue running this study in her IRP lab. She is confident that the resources available at NIH will accelerate her ability to use her discoveries about the microbiome to improve human health.

"The NIH is world-renowned for mechanistic microbiome research," Hourigan says. "Leveraging the highly multidisciplinary environment of the NIH, I am able to take a novel integrative approach to exploring how our microbiomes interact with our physiology and examine the health consequences of clinical microbiome interventions."

ROBERT HUFNAGEL, M.D., PH.D.

National Eye Institute

Shedding Light on Childhood Blindness: Having grown up in a family full of physicians, nurses, and other health care providers, **Robert Hufnagel** has been steeped in medicine all his life. It was not until college, however, that he decided he wanted to spend his life not only treating patients, but also discovering treatments.

"I became fascinated with how vision occurs in the eye and brain, and it became clear that a career in translational science is the way to push forward our medical knowledge of diseases and inspire new therapies," he said.

During the six years that Hufnagel has spent at NIH, mostly in the National Eye Institute with a brief stint at the National Human Genome Research Institute, he has been focused on understanding the genetic underpinnings of ailments that cause blindness in children. This research begins with examining the genomes of children with such conditions to learn which genetic changes might be responsible, after which he examines the effects of those DNA variants on patients' cells or in animal models. Along with his collaborators, Hufnagel has helped identify more than 10 new genes linked to childhood blindness, and he believes they will be able to uncover many more.

"Now, we're looking at larger patient populations and using novel informatics tools to repeat this process for many individuals at once," he said. "By shortening their diagnostic odysseys, we hope that our patients can more quickly learn about their eligibility for new gene-directed therapies."

"The Lasker Scholars program has allowed me to continue building my lab in the NIH Clinical Center, which is the premier research hospital in the U.S. if not the world," he added. "The sequencing and bioinformatics resources, coupled with the ability to translate findings in natural history studies and treatment trials for our patients, present an unparalleled opportunity for precision genomic medicine."

MARIELLE YOHE, M.D., PH.D.

Center for Cancer Research, National Cancer Institute

Pursuing New Treatments for Childhood Cancers: After **Marielle Yohe** lost her grandfather to a heart attack when she was 11 years old, she became determined to help stave off similar misfortunes in other families. As she learned more about the field of medicine, she became particularly drawn to working with children. Eventually, she opted to combine that with her interest in scientific research, which she discovered in high school while working in a biochemistry lab.

"I fell in love with the whole experimental process, from planning the experiment to performing the experiment and finally interpreting the results," she recalled. "I am grateful to have a career that enables me to honor both my passion for clinical medicine and my passion for bench research."

Since her days as a graduate student, Yohe has studied a family of genes called RAS genes. These genes are oncogenes, meaning that mutations in them cause cancer; in fact, mutations in RAS genes are found in as many as 25% of human tumors and up to 90% of tumors in certain types of cancer. As a certified pediatrician, Yohe is particularly focused on exploring the effects of RAS mutations in several forms of cancer that are more common in children than adults. While working as a postdoctoral fellow in the lab of IRP senior investigator **Javed Khan**, she helped identify a specific pattern of modifications to DNA that occur in cancer cells with RAS mutations. These changes were epigenetic, meaning that the DNA itself was not different aside from the mutations in RAS genes, but rather certain chemical tags that change the way other genes behave were more or less concentrated at various locations in the cells' DNA.

"We are only just beginning to understand the implications of that discovery and how it can be leveraged into new therapies," Yohe said.

Now that she has her own lab, Yohe is continuing her efforts to develop new therapies for children with cancer that work by targeting cellular processes related to RAS genes. These efforts include not only laboratory experiments but also clinical trials testing potential treatments in pediatric patients, a combination that is enabled by her access to the NIH Clinical Center. ●

This article, by IRP science writer Brandon Levy, is adapted from a January 24, 2022, post on the "I Am Intramural Blog" at https://irp.nih.gov/blog.

Meet 26 New Stadtman Investigators

Trans-NIH Search Process Recruits Creative, Independent Thinkers

BY LAURA STEPHENSON CARTER

Meet 26 new investigators who were recruited through the Earl Stadtman Tenure-Track Investigators Program, named for renowned biochemist, senior investigator, and mentor **Earl Stadtman** (1919–2008). Stadtman devoted his 57-year career at NIH to identifying the mechanisms of cellular energy expenditure and metabolism. He was chief of the Laboratory of Biochemistry at the National Heart, Lung, and Blood Institute from 1962 to 1994.

The Stadtman program, a trans-NIH search process that crosses all areas of biomedical research, is designed to attract a diverse group of talented early-career scientists who might not apply to NIH via searches conducted by individual institutes and centers (ICs). Stadtman applicants are asked to share their ideas for a novel research program, their career aspirations, and how they would contribute to the NIH mission. For those qualifying, NIH tries to create a tenure-track position in one of the ICs to match that talent.

Two of the Stadtman Investigators featured here are part of the 2017 recruiting cycle and joined NIH in 2021. The 24 other investigators applied in the 2018 cycle and joined NIH in 2019 and 2020.

For more on the Stadtman program, how to apply, and links to stories about other Stadtmans, go to https://irp.nih.gov/careers/trans-nih-scientific-recruitments/stadtman-tenure-track-investigators.

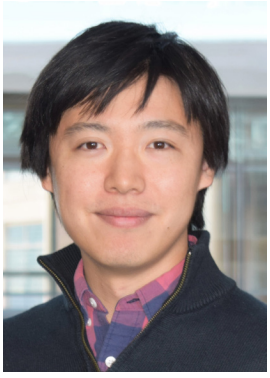
Read a longer version of this article online at https://irp.nih.gov/catalyst/v30i2/meet-26-new-stadtman-investigators.

Applied in 2017 (Became Stadtmans in 2021)

Melissa Brotman, Ph.D. (NIMH)
Neuroscience and Novel Therapeutics Unit, Emotion and Development Branch
Research: Leveraging neuroscience and therapeutics to develop and test novel interventions for serious psychiatric disorders.

Neil Hanchard, M.D., Ph.D. (NHGRI)
Center for Precision Health Research
Research: Using human genetics and genomics to better understand the pathophysiology and etiology of childhood diseases in diverse populations.

Applied in 2018 (Became Stadtmans in 2019 and 2020)



Takashi Akera, Ph.D. (NHLBI)
Research: Using mouse oocytes to reveal the mechanisms underlying meiotic drive, in which selfish genetic elements violate Mendel's Law of Segregation to increase their own rate of transmission.

Benedict Anchang, Ph.D. (NIEHS and NCI)
Research: Performing multiscale modeling, visualization, and integration of dynamic perturbation effects of complex biological processes (in human and nonhuman systems), such as cancer, drug response, or toxicity for precision health.

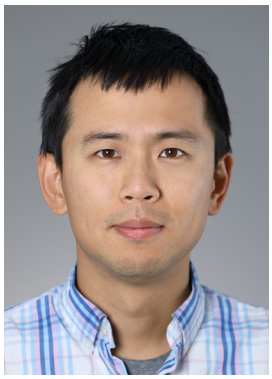
Michelle Antoine, NIAAA

Alexander Cartagena-Rivera, NIBIB

Jiyeon Choi, NCI-DCEG

Erin Davies, NCI-CCR

Jeffrey Farrell, NICHD



Peng Jiang, NCI-CCR

Laurie Krug, NCI-CCR

Michelle Antoine, Ph.D. (NIAAA)

Research: Understanding how genetic and environmental insults affect the computation of neural signals within brain networks to cause neurodevelopmental disorders such as autism, epilepsy, and attention-deficit-hyperactivity disorder.

Alexander Cartagena-Rivera, Ph.D. (NIBIB)

Research: Using both genomics and imaging data to identify new regulators in cancer immune evasion; developing infrastructures that enable users to leverage big data resources to find immune-evasion mechanisms in their own clinical studies and to inform cancer-therapy decisions.

Jiyeon Choi, Ph.D. (NCI-DCEG)

Research: Understanding genetic susceptibility to melanoma and lung cancer; identifying genes and molecular pathways through which heritable genetic variants confer increased cancer risk.

Erin Davies, Ph.D. (NCI-CCR)

Research: Determining the embryonic origin of sustained adult pluripotency and lifelong regenerative abilities in freshwater and marine flatworms; providing paradigms for reverse engineering tissue regeneration in nonregenerative mammalian systems.

Jeffrey Farrell, Ph.D. (NICHD)

Research: Combining single-cell genomics, imaging, genetic, and classical embryological approaches in zebrafish models to investigate the signals and gene expression events that drive cell specification and differentiation during vertebrate embryogenesis.

Peng Jiang, Ph.D. (NCI-CCR)

Research: Using both genomics and imaging data to identify new regulators in cancer immune evasion; developing infrastructures that enable users to leverage big data resources to find immune-evasion mechanisms in their own clinical studies and to inform cancer-therapy decisions.

Laurie Krug, Ph.D. (NCI-CCR)

Research: Applying novel molecular approaches to define the gamma-herpesvirus proteins and host-signaling networks that are required for different stages of infection; conducting mechanistic studies of the virus-host interplay to identify new, effective interventions to treat and prevent cancers driven by Epstein-Barr virus and Kaposi sarcoma-associated herpesvirus.

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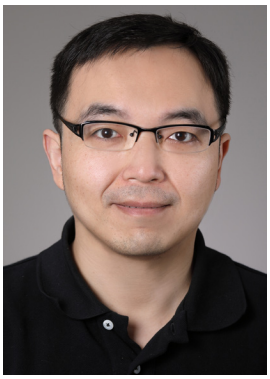
Stadtmans
CONTINUED FROM PAGE 21


Yuanyuan (Kevin) Liu, NIDCR


Emmanouil Maragkakis, NIA


Christian Thomas Mayer, NCI-CCR


Kyle Messier, NIEHS & NIMHD


Naoko Mizuno, NHLBI


Priyanka Narayan, NIDDK


Lauren Porter, NLM

Yuanyuan (Kevin) Liu, Ph.D. (NIDCR)
Research: Deciphering supraspinal circuits in somatosensory perception; investigating underlying mechanisms of top-down control in chronic pain states; determining how our mental states directly alter normal and pathological somatosensory perception; and identifying potential targets for treating pain.

Emmanouil Maragkakis, Ph.D. (NIA)
Research: Understand the high-dimensional regulation of gene expression; identifying mechanistic basis of the physiology and diseases of aging; discovering biological mechanisms that control RNA dynamics.

Christian Thomas Mayer, Ph.D. (NCI-CCR)
Research: Determining regulatory networks controlling cell death in immune-cell development, differentiation, and function; understanding how defects in immune regulation contributes to diseases; identifying new strategies to inhibit unwanted immune responses and enhance immune responses against tumors and pathogens.

Kyle Messier, Ph.D. (NIEHS and NIMHD)
Research: Using methods and applications in spatiotemporal modeling of exposure and risk from environmental, social, and climate variables; applying spatial methods and making explicit connections of human exposure to toxicological models.

Naoko Mizuno, Ph.D. (NHLBI)
Research: Using in situ cellular cryoelectron tomography in combination with techniques such as single-particle cryoelectron microscopy, X-ray crystallography, in vitro reconstitution, and light microscopy to understand molecular mechanisms governing shapes of neurons, activated immune cells, platelets, and cancer cells.

Priyanka Narayan, Ph.D. (NIDDK)
Research: Using techniques from biochemistry, genetic screening, and neurobiology in human-induced pluripotent stem-cell-derived tissues to study how genetic and environmental factors alter fundamental cellular pathways to increase susceptibility or improve resilience to neurodegenerative diseases such as Alzheimer disease; identifying novel therapeutic or preventative mechanisms for neurodegenerative diseases.

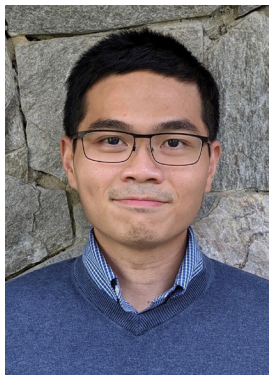
Lauren Porter, Ph.D. (NLM)
Research: Developing data-driven computational methods and using experimental methods to predict and characterize fold-switching proteins, many of which are associated with diseases such as cancer, autoimmune disorders, and bacterial and viral infections.

Kaitlyn Sadtler, NIBIB

Nadine L. Samara, NIDCR

Christina I. Schroeder, NCI-CCR

Han-Yu Shih, NEI



Joshua Tan, NIAID

Kaitlyn Sadtler, Ph.D. (NIBIB)
Research: Understanding how the immune system interacts with medical devices and scaffolds for tissue regeneration; programming immune responses to allow tissue growth and integration with these materials.

Nadine L. Samara, Ph.D. (NIDCR)
Research: Using protein structure, biochemistry, and microbiology to investigate the molecular mechanisms of glycosylation at the host-microbe interface; exploring the role of carbohydrates in the pathogenesis of oral and systemic diseases.

Christina I. Schroeder, Ph.D. (NCI-CCR)
Research: Using peptide engineering of complex bioactive peptides targeting ion channels upregulated in cancer; designing diagnostic tools that unravel the importance of ion channels in cancer.

Han-Yu Shih, Ph.D. (NEI)
Research: Using multidisciplinary genomic approaches to understand mechanisms that regulate gene expression in lymphoid cells; analyzing lymphocyte regulomes to further our understanding of molecular mechanisms that contribute to aging and neurodegenerative diseases.

Joshua Tan, Ph.D. (NIAID)
Research: Studying B cells to identify and characterize human monoclonal antibodies against a range of pathogens; studying basic antibody biology; investigating the use of monoclonal antibodies for prevention of infection and as tools for vaccine design.

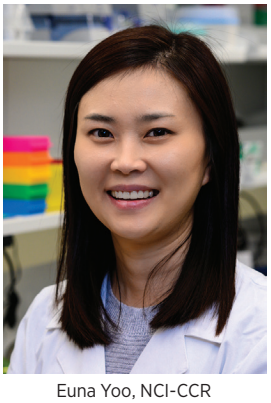
Eugene Valkov, D. Phil. (NCI-CCR)
Research: Unveiling molecular events that determine whether messenger RNA (mRNA) is destroyed, stored, or translated into protein; manipulating mRNA metabolism with precision for therapy.

Jason Watts, M.D., Ph.D. (NIEHS)
Research: Studying how nucleic acid sequences and structures regulate RNA polymerase pausing, and how RNA polymerase pausing contributes to the control of gene expression in response to physiologic and environmental stress.

Euna Yoo, Ph.D. (NCI-CCR)
Research: Discovering novel chemical approaches and molecules that can address immunological problems in cancer therapy; using natural product screening and synthetic chemistry to develop chemical probes that detect and perturb key regulators of biochemical and signaling pathways and enzymes involved in immune activation. ●

Eugene Valkov, NCI-CCR

Jason Watts, NIEHS



Euna Yoo, NCI-CCR

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

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PHOTOGRAPHIC MOMENT

Saying Goodbye to a Statue

CREDIT: MICHELE LYONS, OFFICE OF NIH HISTORY

The Office of NIH History and Stetten Museum (ONHM) recently moved about 3,700 objects in its collection from a storage facility in Rockville, Maryland, to a new one in Gaithersburg. The office's curatorial intern, **Devon Valera**, is holding a "deaccessioned" statue that no longer fits in the museum's collection scope. The not-quite life-size sculpture depicts a child who was the recipient of the first-ever gene therapy on September 14, 1990, at the NIH Clinical Center. The girl had adenosine deaminase deficiency, which left her defenseless against infections. The gene therapy worked. The statue was a prop in a 1996 exhibit at the National Museum of American History and never formally adopted into the Stetten Museum's collection. ●

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

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