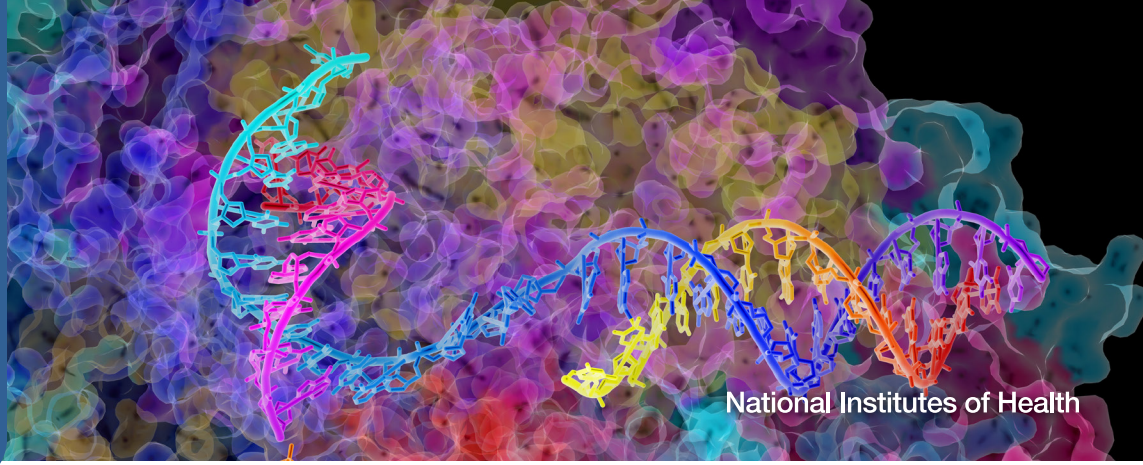
NIH RECORD

May 9, 2025
Vol. LXXVII, No. 10



WONDERS OF THE WOMB

Guardia Studies Role of Environmental Stressors on Fetal Development

BY DANA TALESNIK

Dr. Carlos Guardia is passionate about science. Growing up in Argentina, he was a curious kid, drawn to biology and chemistry from an early age. Encouraged by teachers, inspired by mentors, he became the first scientist in his family. Ten years ago, he found a research home at NIH.

Now, Guardia leads the Placental Cell Biology Group at NIH's National Institute of Environmental Health Sciences (NIEHS), based in Durham, N.C. His team studies the placenta, the first organ of the fetus to develop during pregnancy. The placenta has critical functions; it nourishes and protects the growing fetus. And yet, it's an organ that's relatively understudied.

"The placenta is simple in its cellular makeup, when compared to, say, the brain, but it fulfills so many roles and it dramatically changes during pregnancy," Guardia said.


Dr. Carlos "Charly" Guardia

"I think the most exciting part of my job," he said, "is when my trainees come to me with a finding, and we do investigative research to try to figure out how things work." There's still so much to learn about how the placenta works under normal conditions, he noted, before researchers can figure out how to treat related health issues when they arise.

Guardia's lab studies how different environmental stressors affect placenta development and function.

"We know that's so important because during the early stages of development, if something goes wrong, that could predispose the baby once it's outside of the womb to develop or have a higher risk for certain chronic disorders."

A focus of Guardia's lab is understanding the effects of maternal obesity on the future health of the baby. As a cellular biologist, Guardia is particularly interested in

SEE **GUARDIA**, PAGE 4


Dr. Nora Volkow receives Beacon of Hope award. See p. 3.

ALSO THIS ISSUE

NIH-Supported Network Celebrates a Decade of Advancing Diabetes Research

BY LISA YUAN

At a recent NIH symposium, more than 400 scientists convened to celebrate 10 years of productivity and progress in type 1 diabetes research from the NIH-funded Human Islet Research Network (HIRN). Since 2014, HIRN has contributed groundbreaking insights into the field of type 1 diabetes.

Members of the Human Islet Research Enhancement Center (HIREC) at the HIRN 10th anniversary symposium. From l, Nelly Berger, Layla Rouse, Dr. Denis O'Meally, and Dr. John Kaddis (from City of Hope). **PHOTO: HIREC/HIRN**

"NIH remains committed to supporting the best science," said Dr. Griffin Rodgers, director of the NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). "Through HIRN, we plan to continue to focus on robust science, achieve significant research progress and translate that progress into improving the health of all people."

HIRN aims to understand how beta cells are lost in type 1 diabetes and find innovative strategies to protect or replace these cells in people with the disease. Beta cells, located in

SEE **HIRN**, PAGE 5

Princeton's Cristea to Present Annual Khoury Lecture

May 14

Dr. Ileana Cristea of Princeton University will deliver the annual George Khoury Lecture on May 14 at 2:00 p.m. ET. Titled, "The Virus Microenvironment in 2D and 3D," the lecture will be held in the Lipsett Amphitheater, Bldg. 10 and online at https://videocast.nih.gov/watch=55036.

Dr. Ileana Cristea

Cristea is the Henry L. Hillman Professor of Molecular Biology and director of graduate studies at Princeton. Her research is at the interface between virology and proteomics. Her lab has developed proteomics-based strategies to investigate how viral infections alter cellular processes, with a focus on host-pathogen interactions, immune response mechanisms and organelle remodeling. Her work integrates both targeted and large-scale approaches to map dynamic protein interactions and regulatory pathways throughout the course of infection.

This lecture, part of the Wednesday Afternoon Lecture Series (WALS), honors the memory of the late George Khoury, past chief of the NCI Laboratory of Molecular Virology, who was highly regarded as a superb scientist and caring mentor.

Continuing Medical Education credits will be available. More information about the WALS is posted at https://oir.nih.gov/wals. —**Diana Gomez**

Palsson to Discuss iModulons

May 9

NIH's Office of Data Science Strategy hosts a seminar series to highlight exemplars of data sharing and reuse on the second Friday of each month. The next seminar will take place on May 9 at noon.

Dr. Bernhard Palsson

Dr. Bernhard Palsson, director and principal investigator in the Departments of Bioengineering and Pediatrics, University of California, San Diego, will discuss iModulons.

The first microbial genome sequences appeared in the mid to late 1990s. By the late 2000s, the cost of DNA sequencing dropped massively, leading to rapidly expanding databases of microbial genome sequences and microbial transcriptomes. These data sets could be knowledge-enriched and decomposed into coherently functioning sets of genes using machine learning methods.

Analysis of large biological data sets can take place at four levels. This talk will focus on progress at level 2 with transcriptomes. Large compendia of high-quality RNAseq profiles can now be decomposed using Independent Component Analysis (ICA). ICA identifies independently modulated sets of genes, called iModulons.

This talk will show the uses of iModulons for metabolic engineering and bioprocess development including cross-species transfer of iModulons, media composition, expression of heterologous genes, and y-gene discovery.

The series is open to the public. Registration is required. To learn more and register, see: bit.ly/NIHDataSeminars. Individuals who need interpretating services and/or other reasonable accommodations to participate in this event should contact Allison Hurst (ahurst@scgcorp.com) at 301-670-4990, at least three business days in advance. A recording of the seminar will be posted after the event.

A stream on NIH's Bethesda campus **PHOTO: ERIC BOCK**

NIH Recognizes Earth Day

NIH marked Earth Day on April 22 and encourages staff to take part in ongoing activities that protect the environment, reduce energy consumption, minimize waste generation and contain operational costs to conserve our resources.

NIH programs and materials designed to help staff conserve resources and protect the planet include:

• Participating in the NIH Freezer Challenge to increase the reliability of freezers and reduce the energy consumption from cold storage units. See: https://go.nih.gov/JFvoRiI.

• Using the NIH Solvent Recovery Program and Chemical Redistribution Program to reduce chemical waste and costs. See: https://go.nih.gov/KiGZnEf.

•Reducing medical pathological waste (MPW) and the associated costs through the MPW Totes Program. See: https://go.nih.gov/PPzOUTj.

• Avoiding acquisition costs and waste by reusing equipment and supplies for free with the Excess Product Catalog. See: https://go.nih.gov/a44WlXc.

• Reading the NIH Green Zone newsletter (https://go.nih.gov/Dny4qlH) and watching videos on the ORF YouTube Channel (https://go.nih.gov/Dny4qlH).

Real ID Enforcement Begins May 7

Starting May 7, NIH will only accept state-issued driver's licenses and identification (ID) cards that are compliant with the U.S. Department of Homeland Security (DHS) Real ID Act. This act establishes minimum security standards for state-issued driver's licenses and identification cards to improve their reliability and accuracy.

When using a driver's license to access NIH or any other federal facility, visitors must use a REAL ID driver's license. Current and new employees using a driver's license to obtain a new NIH PIV card will also need to use a REAL ID. Note that all U.S. travelers will be required to use a REAL ID to board domestic flights.

A REAL ID compliant license will have a star in the upper right corner. For more information and to ensure your license is compliant, visit https://www.dhs.gov/real-id/about-real-id.

A full list of approved forms of identification to access NIH campuses can be found at https://go.nih.gov/F8xqkAv.

Volkow Honored at Rx Summit

The annual Rx and Illicit Drug Summit, now in its 14th year, aims to find and implement strategies to prevent drug overdoses and deaths. Synthetic opioids, in particular, continue to claim the lives of tens of thousands of Americans each year.

At this year's summit, held in April in Nashville Tenn., Rep. Hal Rogers (R-KY) presented Dr. Nora Volkow, director of NIH's National Institute on Drug Abuse (NIDA), with the Beacon of Hope award for her pioneering work on addiction and substance use.

A piece of hopeful news announced on the summit's first day was that opioid overdose deaths have declined nationwide by nearly 25% over the past year, according to provisional data from the Centers for Disease Control & Prevention (CDC).

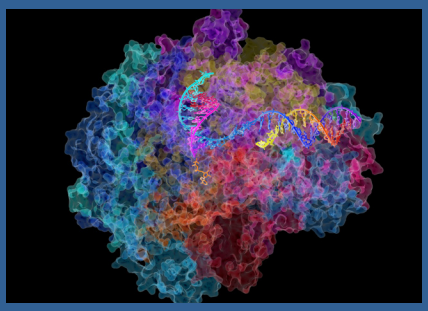
Also on the summit's first day, NIH Director Dr. Jay Bhattacharya delivered remarks. He shared his vision for the agency and affirmed NIH's commitment to continuing research that addresses the opioid crisis.

The Rx Summit brings together government officials, business leaders, doctors, pharmacists, therapists, social workers, law enforcement personnel and others who are committed to solving the opioid epidemic. This year's summit convened more than 180 speakers and featured 160 breakout sessions allowing the many stakeholders to share strategies and discuss concrete ways to put them into action.

For information on NIH opioid research, see: https://nida.nih.gov/research-topics/opioids.

Above l, Dr. Nora Volkow (l) receives the Beacon of Hope award from Rep. Hal Rogers. Above r, NIH Director Dr. Jay Bhattacharya delivers remarks at the Rx Summit in Nashville. Below, from l, Cynthia Doyle, wife of Rep. Rogers; Volkow; Rogers and Bhattacharya at the summit

PHOTOS: OFFICE OF REP. HAL ROGERS



ON THE COVER: *NIGMS-funded researchers solved the structure of RNA polymerase II. This is the enzyme in mammalian cells that catalyzes the transcription of DNA into messenger RNA, the molecule that in turn dictates the order of amino acids in proteins.*

IMAGE: DAVID BUSHNELL, KEN WESTOVER, ROGER KORNBERG, STANFORD UNIVERSITY

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Staff News and Public Inquiries Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email nihrecord@nih.gov.

Editor:
Dana Talesnik • *Dana.Talesnik@nih.gov*

Assistant Editors:
Eric Bock • *Eric.Bock@nih.gov*
Amber Snyder • *Amber.Snyder@nih.gov*

Subscribe via email:
https://go.usa.gov/x6mgQ

Follow: **nihrecord.nih.gov/**

National Institutes of Health
Turning Discovery Into Health

Guardia

CONTINUED FROM PAGE 1

autophagy, the way cells recycle material they no longer need.

"We think autophagy controls and helps the cell recycle when it's under constant stress," he explained. "And we think that's critical. There's evidence that if autophagy is not properly working in the placenta, then the mother can be predisposed to certain pregnancy disorders like preeclampsia."

For their studies, Guardia's lab works with human tissues collected from nearby hospitals from healthy mothers after they've given birth. To study the effects of maternal obesity, they use animal models of pregnancy, feeding mice a high-fat, high-sugar diet. They also have access to trophoblasts, the specialized cells of the placenta, which contribute to the formation of the placenta first and coordinate nutrient exchange to the fetus. Trophoblasts are also important during childbirth.

Inside the womb, Guardia said, the baby's world is whatever the mother provides. The placenta controls how much is needed and required for proper fetal development.

"With maternal obesity, usually there's an abundance of resources and it equips the fetus to survive in an environment of excess nutrients, sugar or fat...[Thus] the placenta may provide many more resources than the fetus actually needs and that could have an impact on future [health conditions]. It could affect heart or brain development or cause predisposition to diabetes, for example, because that's the world the fetus experienced during development."

To that end, one intervention they're studying is whether increased exercise can help compensate for problems or changes in the mother's diet.

"We try to cover the whole breadth of placenta research to tackle basic biology problems that could have translational potential," Guardia said.

Guardia first came to NIH as a Fulbright Scholar in 2013 during his Ph.D. training in structural biology at the University of Buenos Aires. He then conducted postdoctoral research in cell biology with NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). In 2021, he became an NIH Stadtman tenure-track investigator and distinguished scholar with NIEHS.

For aspiring scientists, Guardia advises, "Stay curious, focused and true to yourself."

He said, "Being a scientist requires a lot of self-assessment, self-training and also resilience. Remember that most things fail. So you have to learn how to ride with it, because eventually you may reach the point where you have something novel and innovative."

Guardia also underscored the importance of collaboration and mentorship. "You bring something new, but you also need mentors to help navigate things that may be new for you," he said.

"There's a time for isolating to reflect on your projects and your own ideas," he said, "but there is also a time to seek help and advice to make your dreams a reality."

Guardia (c) poses with colleagues Erixberto Olivencia Alvarez, Dr. Carolina Marvaldi, Keyshla Negron Rios, Elizabeth Padilla-Banks, Guardia, Dr. Asmita Singh, Dr. Ruchir Bobde, Emma Morgan and Maira Perez on the NIEHS campus in Durham, N.C.

CC Biologist Makes Novel Cell Therapies

BY SEAN MARKEY

Dr. Hannah Song

PHOTO: SEAN MARKEY

Dr. Hannah Song and her colleagues at the NIH Clinical Center's Center for Cellular Engineering make novel cell therapies for new medical treatments.

"If an investigator has a new therapy and it involves editing genes or engineering cells outside the body, they can partner with us," said Song.

Her task is to design the process of making that new therapy. One example is CAR T cell immunotherapy, which leverages a patient's immune system to fight cancer.

"We take a patient's T cells from a blood sample in the lab," she explained. "We isolate those cells and put in a gene to better target the cancer. Then we reinfuse those cells into the patient, sending the T cells to destroy the cancer cells."

Figuring out the actual process to engineer those T cells isn't easy. How do they insert the gene? How is the gene activated? What's the best process to handle those cells? A cell therapy is alive. Every step of the process matters. You can't isolate them into powder form like a traditional drug and put them into a pill.

In her own research, Song studies how certain tools may affect cells in unexpected ways. Recently, her team found the oxygen level that T cells are exposed to in the lab seems to play a role in how effective they will be inside the body.

"I love working with cells," she said. "Their ability to sense and respond to their microenvironment and to perform very fine-tuned functions is just incredible. When I learned about cell therapy in my postdoc, that's when I first understood that this is the field I wanted to be in."

Song, who has a Ph.D. in chemical and biological engineering, added, "What's amazing about NIH is the number of researchers who are working on groundbreaking therapies. It's incredible, these world experts who are translating first-in-human studies. My colleagues and I get to help make that a reality.

"I love coming to work every day and collaborating with all the amazing scientists here. They are full of new ideas and never give up on finding a cure. The science is now there to be able to edit cells and provide curative therapies. Instead of treating the symptoms, we can actually cure the disease."

HIRN

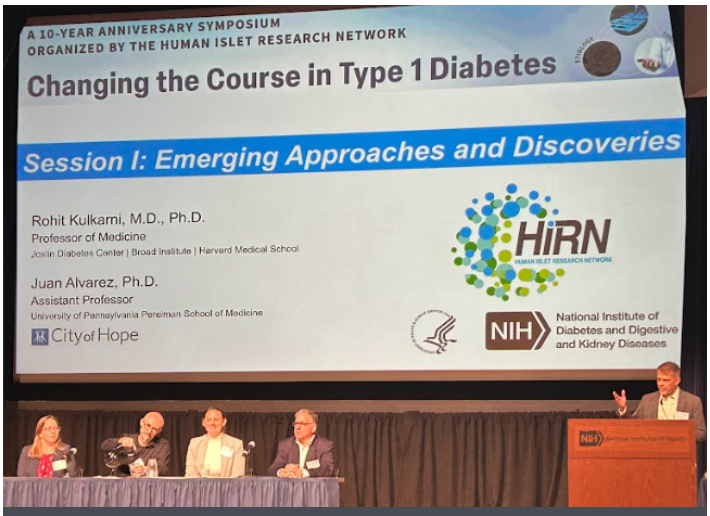
CONTINUED FROM PAGE 1

the pancreas, produce the hormone insulin, which is essential to getting glucose into the body's cells to be used for energy. In people with type 1 diabetes, their immune system attacks and destroys their beta cells, leading to severe insulin deficiency that can be life-threatening.

To achieve its goals, HIRN comprises several complementary consortia, each with its own scientific mission. This structure allows HIRN to evolve as research goals are met, and new opportunities emerge.

"HIRN continues to evolve," said Dr. William Cefalu, director of NIDDK's Division of Diabetes, Endocrinology and Metabolism. "Based on scientific advances, HIRN's scientific consortia, which are focused on specific areas, are merging; new consortia are being implemented, and new initiatives are being discussed to move us into the future. HIRN has been and will remain a key component to inform us on the pathogenesis, detection and treatment of type 1 diabetes."

Since its inception, HIRN has published more than 1,040 scientific papers and made transformative discoveries, including uncovering a new, distinct, early stage of type 1 diabetes and identifying potential therapeutic targets. For example, HIRN researchers found that a blood pressure medication, which targets a protein that is elevated in people with type 1 diabetes and triggers beta cell death, can delay type 1 diabetes progression. Another HIRN study showed that synthetic T cells can be designed to suppress autoimmunity in targeted tissues such as pancreatic beta cells, making it a promising approach to treating type 1 diabetes and other autoimmune disorders.



Dr. Rohit Kulkarni of Harvard Medical School and the Joslin Diabetes Center at podium in a session with HIRN investigators (from l) Dr. Cherie Stabler (University of Florida); Dr. Roberto Mallone (Cochin Hospital, France; Indiana Biosciences Research Institute), Dr. Julia Panzer (City of Hope) and Dr. Adolfo Garcia-Ocaña (City of Hope)

Using the latest technologies, the network has also created valuable resources to benefit the broad scientific community, including an online resource, PanKbase (Pancreatic Knowledge Base), which aims to provide scientists within and outside of HIRN with datasets to help advance knowledge of the pancreas and type 1 diabetes. In addition, HIRN researchers have developed sophisticated mouse models that mimic key features of type 1 diabetes, enabling novel studies on disease mechanisms and preclinical testing of potential new treatments.

Another important priority of HIRN is fostering future generations of diabetes researchers through career development programs and opportunities for collaboration with HIRN scientists. These training and development efforts help ensure that researchers will continue fulfilling HIRN's important mission for decades to come.

At the symposium, early-career researchers and experts from many disciplines—including biology, physiology, immunology, bioengineering and genomics—had opportunities to interact, attend more than 100 poster presentations and share about how their various fields have influenced and will continue to contribute to HIRN's outstanding scientific track record and the type 1 diabetes research community.

HIRN's focus on multidisciplinary and collaborative science, advanced technologies and career development are keys to its success and give promise to more advancements in type 1 diabetes research.

Above, attendees gather at a symposium breakout session; below, attendees network at a poster session in Natcher.

The newly created HIRN Consortia of Modeling Autoimmune Diabetes (CMAD) congregate at the HIRN symposium.

Huffman Gets to the Heart of Mentorship

BY MARIAH FELIPE-VELASQUEZ

During his time in an NIH Fogarty International Center training program, Dr. Mark Huffman analyzed data from more than 25,000 patients with acute coronary syndrome (heart attacks) at 125 hospitals in Kerala, a south Indian state.

India has a high burden of heart disease; optimizing the quality of heart care is critical for improving patients' outcomes.

Dr. Mark Huffman

Before he was given access to the data, Huffman needed to build trust in the Keralan cardiology community. With support from two leading Kerala cardiologists, Huffman traveled around the state, visiting hospitals, meeting with fellow cardiologists, and getting to know his new colleagues. They subsequently planned and executed a trial, funded by NIH's National Heart, Lung, and Blood Institute (NHLBI), that improved the quality of heart attack care in Kerala.

"The Fogarty fellowship was instrumental not only for developing my skills but also for building relationships that could be sustained," said Huffman. One of Fogarty's first cardiology fellows in 2009, he credited his U.S. mentors, Drs. Donald Lloyd-Jones and Robert Bonow, and his international mentor, Dr. Dorairaj Prabhakaran who is based at the Center for Chronic Disease Control in Delhi, for helping him formulate high-impact scientific questions and develop skills, networks and experiences.

Huffman is now the William Bowen Endowed Professor of Medicine and co-director of the Global Health Center at Washington University in St. Louis, with a secondary appointment at The George Institute for Global Health at the University of New South Wales in Australia.

One of Huffman's mentees, Dr. Anubha Agarwal, a former Fogarty fellow and now an assistant professor at Washington University, recently received NIH funding to develop a heart failure polypill in Sri Lanka. Because it addresses a major global treatment gap, her research is as relevant in the U.S. as it is in Southeast Asia.

Another of Huffman's mentees, Dr. Nilay Shah, a professor at Northwestern University, is now leading the MASALA 2G (second generation) study, a follow-up to the parent MASALA (Mediators of Atherosclerosis Among South Asians Living in America) study. MASALA is analyzing the intergenerational transmission of cardiovascular health in South Asians, a population with a higher prevalence of atherosclerotic cardiovascular disease ("hardening of the arteries" caused by plaque buildup in artery walls).

Huffman said, "This study is a great example of why we need to do work internationally, because there are discoveries that can be made and brought back to the United States to help us understand, and also to prevent, treat and control cardiovascular disease, one of the leading causes of death in our country and around the world."

Currently, Huffman is a co-principal investigator of the Cardiovascular Research Training in Nigeria (CeRTIN) program— together with Dr. Lisa Hirshhorn of Northwestern and Dr. Dike Ojji at the University of Abuja. This program aims to strengthen the base of investigators capable of pursuing patient-centered research on cardiovascular disease prevention and control in Nigeria, the most populous country in Africa, which also has a high burden of cardiovascular disease.

Huffman, Ojji, and their teams co-lead several studies in Nigeria that integrate hypertension into routine primary care, evaluate dietary sodium policy implementation and effectiveness, and adapt a U.S.-based home visiting program to improve maternal cardiovascular health.

For Huffman, the most rewarding aspect of his work—aside from growing researchers and creating opportunities through mentorship while working to reduce the burden of heart disease—is seeing long-term benefits for Americans come to fruition.

"When I went to my Fogarty orientation more than 15 years ago, they made sure we all knew we work for the American taxpayer, so when people ask what I do, I say, 'I work for you.'" R

Huffman talks with his mentor Dr. Dorairaj Prabhakaran.

PHOTOS COURTESY OF MARK HUFFMAN

NIH Mourns Passing of Kristie

Dr. Thomas Kristie, an investigator in NIH's NIAID Laboratory of Viral Diseases for more than 30 years and chief of the molecular genetics section since 2001, passed away on March 25 after a long illness.

Dr. Thomas Kristie

Kristie was a pioneer in the field of DNA virus epigenetics and worked on aspects of herpes viral gene regulation and viral chromatin. His work spanned fundamental aspects of gene regulation in vitro to translational research. He was the first to identify specific histone modulating enzymes that could be inhibited to prevent reactivation of herpes viruses in vivo.

He received his Ph.D. from the Committee on Virology at the University of Chicago for his dissertation research with Dr. Bernard Roizman. In this research, he distinguished the promoter sequences of herpes simplex virus immediate-early (IE) promoters from early promoters and identified the host and viral proteins binding to these sequences.

As a postdoc with Phil Sharp at MIT, Kristie showed that host proteins in the aTIF complex included octamer binding factor 1 (Oct-1). He further showed that a host factor, called C-1 or host cell factor 1 (HCF-1), assembles the complex involving VP16 and Oct-1.

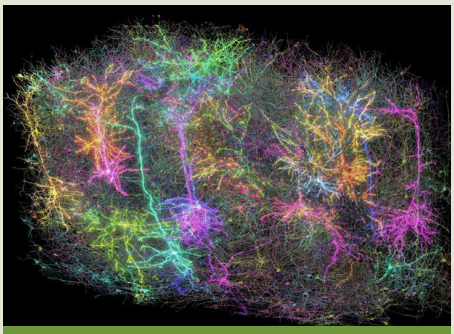
In his own laboratory, Kristie showed that HCF-1 is in the cytoplasm of neurons where it is unable to promote the IE gene transcription of neurons, contributing to establishment of latent infection. He further showed that HCF-1 recruited histone methyltransferases to the IE gene promoters to remove heterochromatic modifications and add euchromatic modifications to histone H3 on the IE gene promoters. He had the idea that blocking removal of the heterochromatin modifications by specific inhibitors would block HSV lytic infection and reactivation from latent infection, which he showed in cell culture and animal models.

Kristie won several awards including the 2009 Norman P. Salzman Memorial Mentor Award in Virology, a 2010 NIAID Merit Award, and in 2012 he was elected a fellow of the American Academy of Microbiology.

NIAID remembers Kristie as a wonderful friend and colleague. He enjoyed organizing the biennial NIH meeting on viral epigenetics, which convenes DNA virologists and chromatin researchers.

In his free time, Kristie enjoyed restoring his house with historic accuracy and was a proud caregiver to several displaced racing greyhound dogs. To share from a book he often quoted, "So long, and thanks for all the fish."

Scientists Map Detailed Connections, Visual Perception in Mouse Brain



This image shows a subset of more than 1,000 of the 120,000 brain cells reconstructed in the MICRONS project. Each reconstructed neuron is a different random color.

IMAGE: ALLEN INSTITUTE

In a massive NIH-funded effort, hundreds of researchers have helped map the connections between hundreds of thousands of neurons in the mouse brain and overlayed their firing patterns in response to visual stimuli. This breakthrough is critical in understanding how our brains process visual information to reconstruct the images we see every day.

The human brain processes information via electrical firing of 86 billion neurons that make trillions of connections with each other. The secrets of how our brain enables us to think, feel and act lie hidden in the complex wiring and barrage of electrical signals that move across it in milliseconds.

While the current findings focus on a tiny fraction of the brain, they reveal the complex connections between the cells and how those connections are wired to produce functional responses.

To carry out the study, researchers presented video clips to mice genetically engineered for their neurons to emit light when they fire. The neuron-firing patterns in areas on the brain surface associated with vision were recorded across a cubic millimeter—about the size of a grain of sand. Within this small amount of tissue lies remarkable complexity: four kilometers of axons, the pathways that nerve cells use to communicate with each other, intertwined to make more than 524 million connections across 200,000-plus cells.

To map these connections, teams worked 12-hour shifts for 12 straight days to carefully cut and image ultra-thin slices of the brain tissue using electron microscopes (EM). Reconstruction required stitching together almost 28,000 EM images. This was followed by months of tracing the connections using deep learning algorithms. A total of 1.6 petabytes of data were collected to create this tiny map, the equivalent of 22 years of continuous HD video.

This information could help us understand how the brain functions, both normally and as the result of various disorders or injuries.

Repurposing a Blood Pressure Drug May Prevent Vision Loss in Inherited Blinding Diseases

New studies in rats suggest the drug reserpine, approved in 1955 for high blood pressure, might treat the blinding disease retinitis pigmentosa. No therapy exists for this rare inherited disease, which starts affecting vision from childhood. A report on the studies, conducted at NIH, was published in *eLife*.

Inherited retinal dystrophies cause degeneration of the retina, the light-sensing tissue at the back of the eye. Vision loss can be present at birth or develop later in early adulthood. Disease progression varies depending on the gene involved. Gene therapies to correct inherited retinal dystrophies are promising but take a long time to develop, are gene specific and often quite expensive.

The findings are the latest evidence that reserpine improves survival of photoreceptor cells, the light-detecting retinal neurons that die in retinitis pigmentosa and other retinal dystrophies.

In their latest work, the NIH research team tested reserpine in a rat model of a dominant form of retinitis pigmentosa caused by a mutation in the visual pigment gene rhodopsin. Compared to untreated rats, reserpine preserved the process by which photoreceptors convert light that enters the eye into electrical signals that are sent to the brain to produce vision.

Unexpectedly, reserpine better protected rod photoreceptors in female rats. The scientists also observed significant preservation of cone photoreceptors in female rats compared to male rats.

The lab is developing additional, more potent reserpine-related drugs. Such options could treat late-onset or slowly progressing inherited retinal dystrophies or simply stall vision loss in aggressive retinitis pigmentosa varieties until more effective treatments are developed that can reverse that vision loss.

Reserpine is no longer used for treating high blood pressure because of its side effects. The required dosage for treating retinal degeneration, however, would be very low and directly delivered in the eye.

AI Screening for Opioid Use Disorder Associated with Fewer Hospital Readmissions

An artificial intelligence (AI)-driven screening tool, developed by an NIH-funded research team, successfully identified hospitalized adults at risk for opioid use disorder and recommended referral to inpatient addiction specialists.

GROUND PICTURE/SHUTTERSTOCK

The AI-based method was just as effective as a health provider-only approach in initiating addiction specialist consultations and recommending monitoring of opioid withdrawal. Compared to patients who received provider-initiated consultations, patients with AI screening had 47% lower odds of being readmitted to the hospital within 30 days after their initial discharge.

The study, published in *Nature Medicine*, demonstrates AI's potential to affect patient outcomes in real-world healthcare settings and suggests investment in AI may be a promising strategy.

In a clinical trial, researchers compared physician-led addiction specialist consultations to the performance of their AI screening tool. Researchers first measured the effectiveness of provider-led consultations. They then implemented the AI screening tool to assist the healthcare providers and remind them throughout hospitalization of a patient's need for an addiction specialist's care.

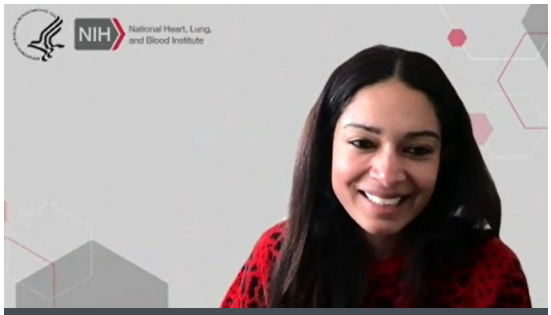
The AI screener analyzed information within all the documentation available in the electronic health records in real time, such as clinical notes and medical history, to identify features and patterns associated with opioid use disorder. Upon identification, the system issued an alert to providers when they opened the patient's medical chart with a recommendation to order addiction medicine consultation and to monitor and treat withdrawal symptoms.

The trial found no decrease in quality with the AI-prompted consultation, which offered a more scalable and automated approach.

However, challenges remain, including potential alert fatigue among providers and the need for broader validation across different healthcare systems. Future research will focus on optimizing the AI tool's integration and assessing its longer-term impact on patient outcomes.

NIH Investigator Discusses Heart Health

BY CAROL JABIR



Dr. Ayesha Siddiqui discussing heart health

National Heart Month is celebrated in February each year, but protecting our hearts is a year-round process. Recently, Dr. Ayesha Siddiqui, a family medicine doctor and perinatal epidemiologist, spoke to NIH staff about heart disease prevention, during which she shared heart-healthy tips that can be implemented all year long.

Cardiovascular disease (CVD) is the leading cause of death and disability around the world. It's the most frequent cause of death in the United States among people 45 and older. And yet, the vast majority of CVD is preventable.

Siddiqui's talk focused on understanding cardiovascular risks and adopting heart-healthy habits, based on the most recent recommendations for primary prevention from the American Heart Association and the American College of Cardiology. Siddiqui, program director of the Clinical Applications and Prevention Branch in the Division of Cardiovascular Sciences at NIH's National Heart, Lung and Blood Institute (NHLBI), discussed the ABCDEs of heart disease prevention: assessing risk; blood pressure control; cholesterol management; diet, exercise and screening.

Assessing Risk

There are several well-established risk factors for CVD including high blood pressure, high blood cholesterol; excess body weight and obesity; prediabetes or diabetes; smoking and lack of regular physical activity.

Age is also a risk factor: 55 or older for women, 45 or older for men.

Each one of these risk factors increases the chance of developing heart disease. The more factors, the higher the overall risk because the factors work additively, noted Siddiqui, so it's important to understand them to help assess individual risk.

There are also risk-enhancing factors. Siddiqui noted these are more nebulous, but they have quite a bit of data behind them. These include family history of premature CVD, particularly a close relative; metabolic syndrome; chronic inflammatory conditions; chronic kidney disease; history of premature menopause and/or pregnancy-associated hypertensive disease (preeclampsia). Another risk-enhancing factor is primary hypercholesterolemia, a rare genetic disorder, unrelated to dietary intake, which predisposes an individual to CVD risk.

Some risk factors are non-modifiable; after all, people cannot change their genetics. But there are modifiable factors that are in our power to change or implement in caring for own cardiovascular health, after consulting a primary care doctor or cardiologist.

A note of caution about a previously accepted prevention strategy: Most data shows the risks of taking aspirin outweigh the benefits, so aspirin is generally not recommended for primary prevention, or to take preemptively, except in rare cases.


PHOTO: STOCK CREATIONS / SHUTTERSTOCK

Blood Pressure

High blood pressure (hypertension) is the leading cause of CVD-associated death. Blood pressure can be influenced by genetics, weight, diet, smoking, alcohol intake, physical activity or stress.

Normal blood pressure shows systolic (upper number) as less than 120, and the diastolic (lower number) less than 80. Siddiqui noted that the latest AHA-ACC guidelines show a correlation between increased blood pressure, alcohol and cancer risk. Research shows that even moderate alcohol intake raises BP, which can increase CVD risk.

Cholesterol

The human body makes all the cholesterol it needs naturally. So the recommendation is to eat as little dietary cholesterol as possible. Dietary cholesterol is found in animal foods, including meat, seafood, poultry, eggs and dairy products.

Diet

A heart-healthy diet includes vegetables, fruits, nuts, whole grains, vegetables or lean animal proteins and fish. The recommendation is to avoid trans fats and limit red meat and processed meats refined carbohydrates and sweetened beverages. The DASH diet—developed by NHLBI— is designed to lower blood pressure and improve heart health.

Exercise

On average, people spend 7 hours a day working in front of a screen. The key is to replace screen time, when possible, with physical activity.

For physical activity, aim to get at least 150 minutes of moderate-intensity aerobic activity each week, or 90 minutes of vigorous-intensity exercise. The key is to get your heart rate up while exercising.

For those who are more sedentary, the objective is to incorporate moderate-intensity exercise when possible. For example, Siddiqui said, while at work, take the stairs instead of the elevator or take a walk.

Other lifestyle factors to keep in mind: elevated stress and inadequate or irregular sleep can also be CVD risk factors.

Siddiqui shared a list of cardiovascular questions to ask at an annual checkup. They include:

- What is my risk of developing heart disease?
- What is my blood pressure and, if elevated, what do I need to do about it?
- What are my cholesterol numbers and what do they mean to me?
- How much physical activity do I need to help protect my heart?

Getting a handle on risks and family history can lead to a personalized approach to preventing heart disease.

"The most important way to prevent heart disease is with a healthy lifestyle starting at a young age and throughout life," Siddiqui said. Viewing cardiovascular health as a continuum can help us to achieve our goals and make each day count.