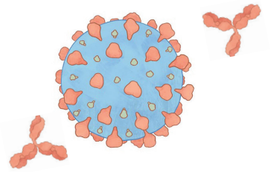
THOMAS JEFFERSON UNIVERSITY

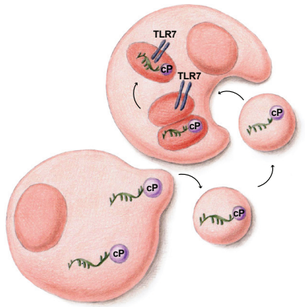
RESEARCH

A Path to Digital Equity

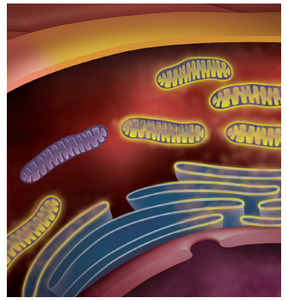
Inside this issue / No. 3



EDITORIAL

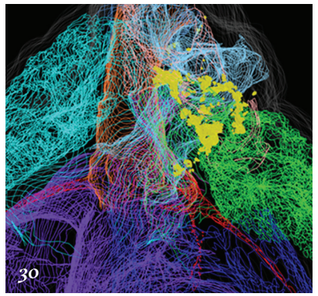


METHODS

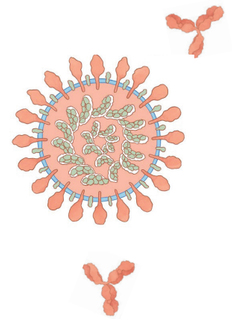


FEATURES

BRIEFS



PORTRAITS



Thomas Jefferson University Research Magazine
Brought to you by:

Mark L. Tykocinski, MD
Provost and Executive Vice President
Thomas Jefferson University

Patricia M. Baldridge, MBA
Senior Vice President, Marketing and Communications

Editor
Edyta Zielinska, MS, MfA

Features Editor
Karuna Meda, PhD

Art Director
Barry Smith

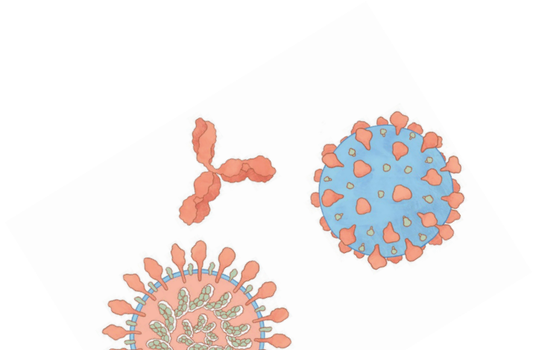
Designer
Denise Hansen

Writers
Karuna Meda
Merrill Meadow
Roni Dengler
Edyta Zielinska

Cover Art
Erin K. Robinson

Photographers
Britney Lillya
Karen Kirchhoff

Illustrators
Joana C. Carvalho
Traci Derberko
Thom Graves
Monika Jasnauskaite
Erin K. Robinson



BUILDING *the* RESEARCH ENTERPRISE *of* 2028

This edition of *Jefferson Research* offers a tantalizing peek at the array of work done at Thomas Jefferson University: from how mitochondria communicate with nearby organelles, to the use of innovative textiles to reduce a building's energy consumption; from how "digital readiness" can improve health equity, to space travel's effects on the immune system.

It also serves as a lens on the exciting path that the our university's research community will pursue over the next five years, guided by our new strategic plan for the Jefferson Research Enterprise. The carefully calibrated plan draws on insights from faculty, students and staff across the institution. It is rooted in the University's overarching tripartite objective: Before decade's end, Jefferson will be recognized as a national research university distinguished by programmatic excellence, innovation and multidisciplinary, multi-sector partnerships. We will be seen as the model for professions-focused higher education. We will be a distinctive, robust global presence in research and education.

Our research strategy builds on our nearly 200-year legacy of pioneering achievements in education, scientific discovery and technical invention. Excellence, innovation and collaboration are woven through the four core elements of our strategic plan.

First, we will leverage the programmatic research themes we have developed over the past decade to create or expand a select number of centers of research excellence (CRE). Prioritized by their potential for scientific and social impact, the CREs will address fields ranging from Smart and Healthy Cities to Life Energetics to Small RNA Discovery to Fashion and Textile Futures — and will include continued expansion of research at our NCI-designated Sidney Kimmel Cancer Center — Jefferson Health, the Vickie & Jack Farber Institute for Neuroscience, and the Computational Medicine Center, as well as launch of a Center for Vaccines and Pandemic Preparedness and an Institute for Global Health Security.

At the same time, we will continue advancing the work of individual scholars and small teams as they create and apply knowledge across a broad range of subjects: from investment banking practices, to the psychological roots of conspiracy theories; from sustainable architecture to racism in news media; from dissemination of Africa-based scholarship to the roots of creativity, and to women as entrepreneurs. (You'll find examples of this exciting and impactful research in the pages of this magazine.)

Second, replicating the success of the Jefferson Institute for Bioprocessing, we will launch a series of education-based initiatives that have significant research and development components. Those initiatives will leverage the rich potential — and Jefferson's existing strengths — in areas such as Heatlh Cybersecurity, Biocomputation Human Factors Engineering and Design Thinking.

Third, we will continue growing our clinical research program (which now has more than 1,300 active clinical trials), aiming to increase patient participation by 50 percent. Toward that goal, we will build programs to address the specific needs of Jefferson's communities through targeted trials addressing clinical challenges such as stroke, cardiac disease and diabetes. This initiative is just one facet of a cross-cutting commitment to expand population science research across the University—especially the kind of work that will enable us to understand and counter the roots of health disparities.

The new relationships we create with our local communities will be the cornerstone of the fourth core element of our research plan: expanded partnerships and collaborations. We will, for example, launch regional partnerships to access high-end technologies; and catalyze national consortia to pursue targeted, high-impact research challenges. Of course, we will also expand the research programs undertaken by our seven Jefferson global centers and Consortia and by investigator-driven collaborative studies in 23 countries. With our partners, we will continue to address challenges ranging from maternal and infant death in India to road traffic injuries in Rwanda; and pursue collaborations that open new horizons — such as our work with investigators in Israel on biomedical projects to be undertaken on the International Space Station, and our robotics and artificial intelligence research in Japan.

Over the past decade, building on our predecessors' achievements, we have fortified the foundation of a truly extraordinary research enterprise. That foundation includes a world-class faculty, state-of-the-art core facilities and an energetic culture of team science and interdisciplinary exchange. We have established strong seed- and bridge-funding mechanisms and garnered steadily increasing external support: since 2017, our research revenue from agencies, corporations and foundations has grown by more than 64 percent. The dynamic expansion of our discovery and scholarship is reflected in a quadrupling of our publications to over 4,000 this past year.

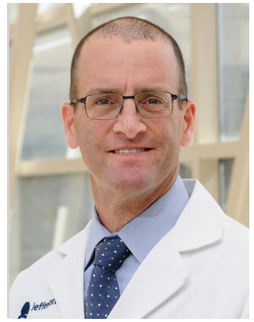
In reading this magazine, I think you will see why we are so proud of what we have accomplished, and so enthusiastic about the future of Jefferson's research enterprise. I firmly believe it will be a future of both profound discovery and truly beneficial impact for our community and our world. ■

Mark L. Tykocinski, MD
Executive Vice President, Academic Affairs
Provost, Thomas Jefferson University
Anthony F. and Gertrude M. DePalma Dean
Sidney Kimmel Medical College

Programmatic Research

"Programmatic, basic and translational studies are the bedrock of scientific research at Jefferson, and we are continuing to build on our areas of great strength. These include nationally recognized programs in cancer mechanisms and immunotherapies, neurodevelopment and neurodegeneration, infectious diseases and vaccines, fibrotic disease and RNA biology. We will launch other initiatives in highly promising areas as well — and, working across disciplines and disease areas, we are committed to having real impact in reducing disparities in care and addressing the nonbiological causes of disease. To empower our investigators, we will continue making major investments in new research technologies — capitalizing, for example, on recent acquisitions of flow cytometry and cryo-EM systems, expanding our bioinformatics infrastructure, and making large-scale additions to the laboratories and core facilities available to our investigators." ■

Steven B. McMahon, Ph.D.
Senior Associate Provost for Programmatic Science



Clinical Research

"Clinical research brings the leading edge of our knowledge and scientific creativity directly to patients to improve medical care. Over the next five years, we will continue to empower our physicians and other investigators to advance new and better ways to promote health and detect, diagnose and treat disease. To that end, we will encourage substantially more faculty to engage in clinical research, in several ways: first, by expanding the successful "Clinical Research Boot Camp" for new clinician-scientists; second, by offering more Emerging Medical Science awards, which provide protected time for early career investigators; third, by increasing internal funding for pilot projects that translate faculty research into real interventions. We will also build infrastructure, such as the Jefferson Health Informatics Core, to help investigators organize and analyze electronic health records in ways that yield population-level insights and point the way to community-focused clinical research initiatives." ■

David Whellan, MD, MHS
Senior Associate Provost for Clinical Research
James C. Wilson Professor of Medicine

Applied Research

"At Jefferson, the term 'applied research' has broad application. It ranges from studies of soft materials and surface imaging to antitrust laws' effect on foreign investment. It includes academic-corporate partnerships where our industrial designers investigate and develop solutions for real people's challenges, and multidisciplinary projects with concrete impact—such as our initiative that bridges political science, economics, management, and materials science to help develop a sustainable and profitable hemp-based industry.

"In the next few years, we will expand our core capacities to do intellectually rigorous, impactful applied research by providing more bridge and project-completion grants to faculty, expanding dedicated research space on our East Falls campus, and increasing funding for graduate research and technical staff. With those resources, we will grow an array of already strong programs in areas such as business structure and supply chain modeling, product design and development, sustainability and building systems, and textile and materials technology." ■

Ronald Kander, PhD
Associate Provost for Applied Research

Reaching Across the Globe and to the Stars

From maternal health to science in space, Jefferson's global initiatives are attacking pressing problems through connected learning and investigation.

BY **EDYTA ZIELINSKA (ESZ)**

Research blooms in an interconnected world. Research that is open to the rich knowledge, experience and culture of collaborators across the globe is stronger for it. Thomas Jefferson University is building international partnerships to tackle health disparities and innovations in medicine, and to broaden access and opportunities that have lasting impact. Read about Jefferson's global footprint.

Africa Coalition

The Jefferson Consortium of African Partnerships (JCAP) forms multi-institutional partnerships with African colleagues in academia, industry and government in pursuit of a healthier, equitable, resilient African future. Led by Chris Harnish and Lauri Romanzi, MD, JCAP includes collaborations with faculty and students across the continent, with in-depth institutional-level partnerships in Rwanda and Malawi. In Rwanda, JCAP is working on initiatives to improve road traffic and reduce crashes and injuries. Elizabeth Krebs, MD, has supported Rwandan institutions to win road-safety funding from the United Nations Road Safety Fund and Global Road Safety Facility of the World Bank. Chris Harnish leads the Malawi Health and Design Collaborative in partnership with the two largest tertiary teaching and research hospitals in the country. They have developed safer care models for infectious disease units and are currently working on designs for the first regional teaching hospital in the country.

India Centers

The biggest contributors of maternal and infant death worldwide are blood loss during childbirth, hypertension during pregnancy and preterm birth. In a landmark clinical trial, India Center director Richard Derman, MD, and his research colleagues in the U.S. and India, along with members of the NIH-funded Global Network for Women's and Children's Health, showed that daily low-dose aspirin could safely decrease the risk of preterm birth by 11%. The trial included nearly 12 thousand women in India, Pakistan, Guatemala, Democratic Republic of the Congo, Kenya and Zambia. His prior work also showed that misoprostol, a common and inexpensive lipid hormone, could reduce blood loss during childbirth. Now Dr. Derman and his global collaborators are attacking anemia in the RAPIDIRON trial; anemia affects 50% of pregnant women in India and is a strong contributor to both maternal death and neurodevelopmental outcomes in the children of affected women.

Ireland Center

The University has formed a working partnership with University College Dublin (UCD), Technological University Dublin and Ulster University in Northern Ireland to focus on global issues where interdepartmental infrastructure already exists, and where faculty have globally recognized expertise. The eight content areas for exploration include architecture and the built environment, autism spectrum disorders, maternal child health, eye diseases health disparities, nutritional sciences, digital health and technology applications. Each of the European partner institutions has a history of having received HORIZON funding for collaborative research, as well as ERASMUS funding to promote student exchanges. The Jefferson Institute for Bioprocessing (JIB) was developed by a model created in Ireland. A joint collaboration with the College of Architecture and the Built Environment (CABE) is being explored to expand SMART Labs, a doctoral program developed at UCD which grants PhDs credits for practical life experience. An expanded academic partnership, which includes Wills Eye Hospital links new innovation to address the leading causes of blindness globally.

Italy Center

The Italy Center, led by Ignazio R. Marino, MD, is the first to offer a joint and unprecedented program granting students a double MD degree valid both in the U.S. and Europe, as well as a Master in Population Health. The Center is also home to a unique MS program in fashion design management that draws from collaborations with major Italian universities and companies. Italy Center programs draw international funding and foster collaboration across borders, including joint clinical trials on vascular surgery and stroke/Parkinson's, and a partnership aimed at building a new Institute of Neuroscience in Rome.

Israel Center

Led by Zvi Grunwald, MD, at Jefferson, the Israel Center focuses on collaborations with innovation and life-science industries as well as leading academic and medical centers in Israel. One set of collaborations is poised to send Jefferson research to the International Space Station (ISS) aboard the Rakia mission, the first private mission to the ISS. Three projects will examine the impact of space on the human body, specifically: the effects of mission-induced stress; changes in the urinary microbiome; and how space travel affects the immune system.

Japan Center

The Japan Center, led by Charles Pohl, MD, has been forging collaborations with several institutions in Japan in the realms of education, research and clinical care innovations. One partnership explores pandemic-related challenges and new opportunities in undergraduate nursing education between Japan and the U.S. Researchers at Jefferson and in Japan are evaluating opportunities for synergistic collaboration in various academic disciplines, including aging, rehabilitation medicine technology, telemedicine applications, robotics and artificial intelligence. Jefferson is also working with Toyota and Canon to advance new educational initiatives for students in design thinking, innovation and population health. Finally, the Center is proud to be hosting researchers from Japan, who are currently at Jefferson working with expert PIs in the fields of ischemia/reperfusion injury, resuscitation science and artificial intelligence/learning.

Latin America Consortium

Projects in the planning phase include the creation of collaborative faculty development initiatives with Universidad de Los Andes in Bogota, Colombia. Ongoing projects include a new medical student case-based learning initiative currently being tested with Universidad CES in Medellin, Colombia. There are additional longitudinal clinical research initiatives in the area of infectious disease with partners in Peru.

Bursts *of* Power

Mitochondria fire oxidants to communicate with organelles nearby, a communication that could be important in various diseases.

BY **EDYTA ZIELINSKA** | ILLUSTRATION BY **THOM GRAVES**

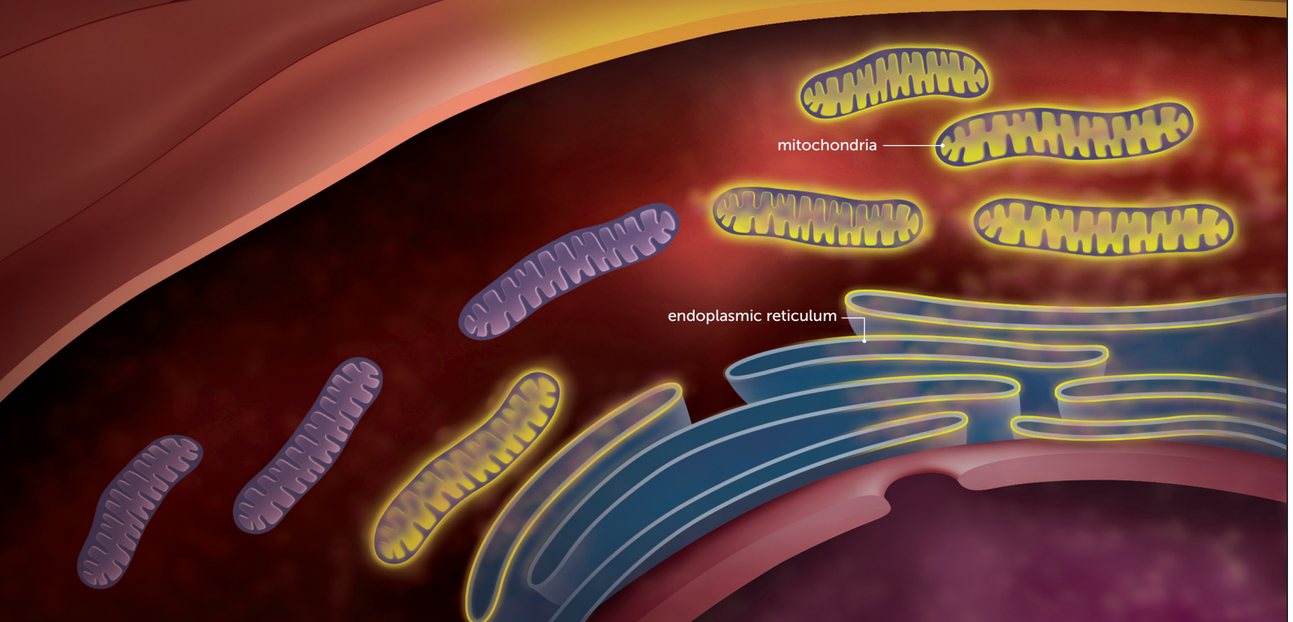
For a few years now, researchers have noticed that clusters of mitochondria abruptly change their activity inside the cell: a smattering firework here, a few there, all seemingly random. When at rest, only a few light up. But when the cell is stressed, it's like a meadow full of fireflies at dusk. What do these fireworks mean for the cells? Gyorgy Hajnoczky, MD, PhD, the Raphael Rubin, MD, Professor of Pathology, Anatomy and Cell Biology, and his team at the Jefferson MitoCare Center developed a toolkit of ultra-resolution instruments and fluorescent tags to find out what was happening at the individual-mitochondrion level, and discovered a mechanism for messages whispered only to the closest of neighbors. While oxidation drives energy production, it may also be involved in a new and highly specific kind of communication.

In recent years, researchers from fields as far flung as neurology, genetics and ophthalmology have found a role for mitochondria in disease. More than 3500 papers, including work from Dr. Hajnoczky, have linked mitochondria to Alzheimer's disease alone, and the organelle likely plays a role in nearly every other neurodegenerative disease. Although many researchers agree the mitochondria are involved, they don't yet know exactly how.

A recent study published by Dave Booth, PhD, Dr. Hajnoczky and collaborators in the high-impact journal *Molecular Cell*, uncovered a means of specific communication that could explain how mitochondria is involved in disease. The researchers show that mitochondria send messages to neighboring organelles, usually the endoplasmic reticulum — the site of protein and phospholipid production and calcium storage in the cell — and the organelles answer back. Mitochondria discharge oxidants that trigger the endoplasmic reticulum to release calcium. Rather than broadcast to the entire cell, however, these missives are only meant for organelles in closest proximity. The rest stay in the dark. But when the cell becomes stressed, the mitochondria amplify the whisper into a full-scale broadcast meant for the entire cell.

What is the use of the messaging for the mitochondrion and for the cell? Mitochondria are clearly initiating a conversation, and the Hajnoczky lab is working to find out whether these signals help to maintain the local status quo and whether the amplification and expansion of the signals could be involved in diseases like neurodegeneration. ■

Mitochondrial Whispers and Shouts
A single mitochondrion flickers on with an oxidative burst (bottom left). It sends a signal to its closest neighbor — the endoplasmic reticulum, which answers back, without alerting other organelles. But under stress (right), as in disease states, these same oxidative messages are amplified and broadcast to the entire cell in a global alert.



ILLUSTRATIONS BY **JOANA C. CARVALHO**

Antitrust Laws Don't Hinder Foreign Investment

BY **KARUNA MEDA (KM)** AND **MERRILL MEADOW (MM)**

Foreign investment capital is key to building robust economies in developing countries. Many factors influence a nation's ability to attract such investment, ranging from political transparency and bureaucratic efficiency to inflation and taxation. "Most of those factors have been studied extensively," says Raju Parakkal, PhD, associate professor of International Relations. "But little research has explored the effect of pro-competition laws on foreign investment in emerging economies, despite their widespread adoption."

Dr. Parakkal, who studies the interactions of policy, politics and economy, believed it was urgent to begin filling that research gap. Therefore, he undertook a comprehensive analysis of the effect of national competition laws on 155 emerging economies. Using data on the period from 1970 to 2019 from the World Bank's World Development Indicators, he considered the question of whether anti-trust laws encourage or diminish foreign investment in developing and transition countries.

His findings strongly suggest that foreign investment is associated with countries that employ pro-competition laws, even after controlling for other possible determinants of these capital flows. "There is overwhelming evidence that competition laws promote foreign investment in these emerging economies," says Dr. Parakkal. "Our analysis demonstrates that multinational corporations, while being apprehensive of the possible misuse of competition laws, generally see long-term positive effects of these laws on their investments in emerging economies. Moreover, these businesses expect the administration and enforcement of national competition laws in new jurisdictions to ultimately pivot to a more pro-market disposition — if they were not so from the beginning."

Dr. Parakkal hopes that his study's finding will inform policymakers in developing and transition countries about the importance of competition laws in encouraging foreign investment in their economies. And he advocates for research into other little-examined factors that could have significant effect on foreign direct investment. ■

Cancer Prediction Model Misses High-Risk Black Patients

Black men are more likely to die from lung cancer than persons of any other racial or ethnic group. A new study suggests that better detection could reduce that disparity.

"Black individuals develop lung cancer at younger ages and with less intense smoking histories compared to white individuals," says the study's leader, Julie Barta, MD, assistant professor in the division of Pulmonary and Critical Care Medicine.

Patients referred for lung cancer screenings are otherwise healthy, but identified by their doctors as being at high risk via algorithm-based risk prediction models derived from data that includes just five percent or fewer Black individuals.

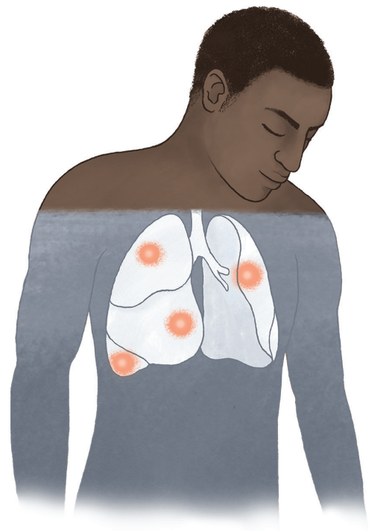
Dr. Barta and team found that a commonly used risk prediction model—the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial modified logistic regression—does not identify many high-risk Black patients who could gain life-saving benefit from early screening.

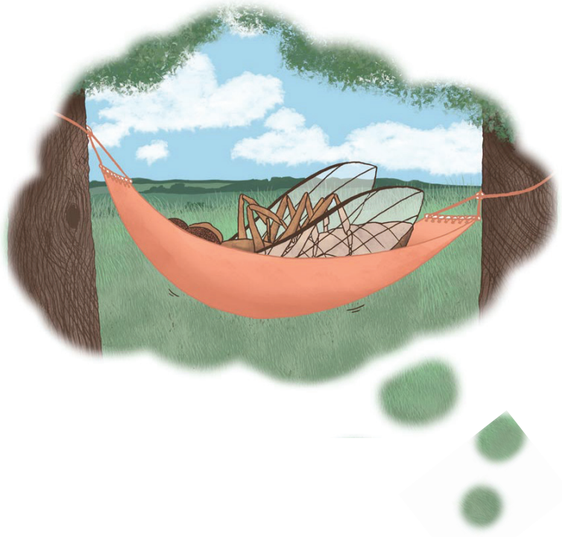
The finding emerged from the team's cross-sectional, retrospective study of 1,276 Black and white patients enrolled in the Jefferson Lung Cancer Screening Program. It found that white patients with screen-detected lung cancer generally had high lung cancer risk scores; and, theoretically, there should have been a similar finding among Black patients. However, the researchers found that despite having a definitive lung cancer diagnosis, Black patients were actually defined by the model as lower risk.

"The study leads us to suggest multiple changes in the present approach," Dr. Barta says. "For example, criteria for lung cancer screening should be expanded to include more diverse populations; and risk-calculation models should include factors such as environmental contributors, access to health care, and other social determinants of health."

"Our research is an important step toward reducing disparities in screening and early detection of lung cancer," she observes. ■

KM, MM





Learning from Drowsy Flies

Who knew that fruit flies slept—or that humans might benefit from studying their sleep? Kyunghee Koh, PhD, does. The associate professor of Neuroscience uses fruit flies (*Drosophila melanogaster*) to identify the cellular and molecular mechanisms underpinning sleep. Two of her lab's recent studies offer results that are both interesting and potentially far-reaching.

The first study explored a phenomenon most humans experience: being lulled to sleep by motion or vibration. "Babies like to be rocked to sleep, but the neural mechanisms underlying this phenomenon remain largely a mystery," Dr. Koh explains. "We used the fruit fly to study the mechanisms of sleep induction via vibration."

The researchers found that flies sleep longer during vibration; are less responsive to light pulses that would otherwise wake them; and are better able to function well with less sleep afterward. They also discovered that the amount of extra sleep during vibration depends on flies' genetic background.

The second study explored sleep-related decision making. "The fly brain is constantly doing a sophisticated cost-benefit analysis of what behaviors to pursue in particular circumstances," Dr. Koh says. In the latest of a series of studies on decision making, the researchers looked at how the need for food would affect fruit flies' choice of whether to sleep or mate. Male flies that were deprived of an important source of protein chose sleep; their well-nourished counterparts chose to mate.

"It turns out protein is necessary for flies' offspring to survive," explains Dr. Koh. "So, these malnourished males decided that even a successful mating was less likely to produce live offspring, and chose sleep over courtship." The findings of this study offer new paths for the Koh lab's continuing exploration of the molecular basis of behavior. ■ KM, MM

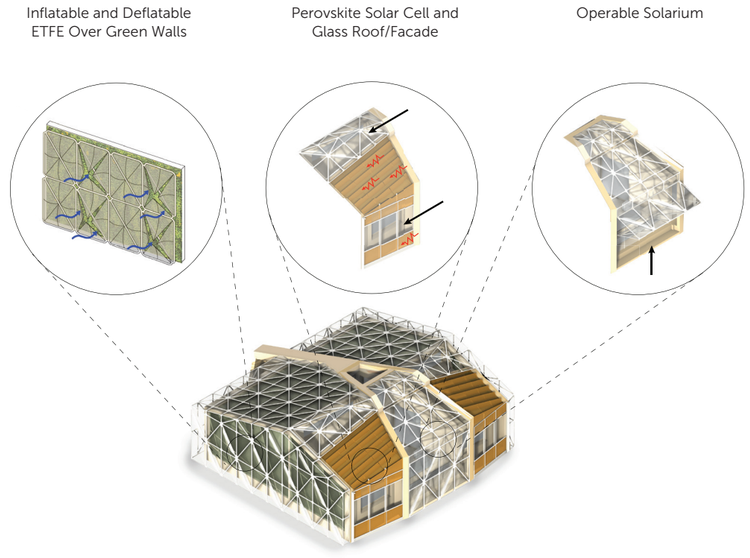
A student team guided by Dr. Ku designed a building envelope, in collaboration with academic partners in China for the Solar Decathlon 2021 Design Challenge. Details of the adaptive structure are shown below.

Enveloping Buildings in Textiles

There are myriad elements that determine how well a building functions. One of the most important and complex is the design and composition of its envelope. Similar to the human skin, the building envelope is the boundary between interior and exterior, and it has multiple functions: protecting the indoor environment, facilitating climate control and reducing the building's energy consumption.

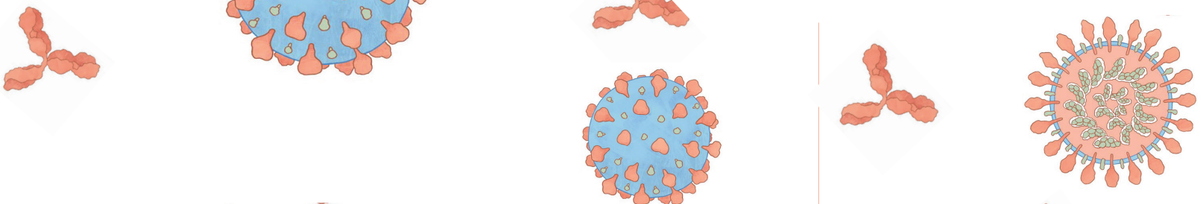
Kihong Ku, DDES, associate professor of Architecture, broadly focuses on how technology empowers designers to enhance design capabilities. Currently, he's working to improve building envelopes through innovative application of textile materials, using advanced computational design and fabrication technologies.

"Building envelopes have come a long way from when stone and brick were used for both a building's structure and its skin," Dr. Ku explains. "Today, we are developing envelopes made of textiles—such as fiber-reinforced composites and fabric- or foil-membranes—that enable the expression of lightness and controlled transparency and that meet growing requirements for 'intelligence' and sustainability."



Dr. Ku is investigating how to take full advantage of emerging innovations in textiles and fibers. For example, he is developing reconfigurable mold systems that enable cost-effective production of complex-shaped fiber-reinforced composite panels for building envelopes. He is also working on adaptive building envelope systems that use embedded sensors and actuators to adjust shading and ventilation mechanisms in response to changing temperature, sunlight and weather conditions.

"My projects take advantage of cutting-edge computational design and fabrication technologies," Dr. Ku says, "but, frequently, they also depend on interdisciplinary collaborations with colleagues and students in textile design and textile engineering. These partnerships have been very fruitful: We have developed new forms or techniques for making things; but more than that, we have learned to bridge our disciplines' fundamental thought processes, creating new approaches that integrate those distinct ways of thinking." ■ KM, MM



COVID Briefs

Intellectual Disability a High Risk for COVID-19 Death

Early in the COVID-19 pandemic, researchers realized that people over 65 were more likely — 80 times more likely — to die from a COVID-19 infection than younger patients. As the pandemic continued, other risk factors emerged: underlying health conditions and those from racial and ethnic minority groups. Mary Stephens, MD, Wendy Ross, MD, and colleagues were interested in whether having an intellectual disability might be a risk factor also. To find out, they analyzed a massive dataset of nearly 65 million patients infected with COVID-19, in a study published in *NEJM Catalyst*. Their analysis showed that having an intellectual disability put people at the highest risk for COVID-19 infection and second-highest risk for death from the disease, after older adults. As a result of the study, patients with intellectual disabilities were prioritized for vaccination. ■ ESZ

Design Solutions for COVID-19 Problems

Jefferson's focus on design thinking and innovation paid dividends during COVID-19, when hospitals, including our own, were hit with shortages in everything from hospital gowns and full-body protective coverings, to masks and childcare for essential workers. Collaborating across disciplines, doctors and designers, textile experts and frontline workers came together to come up with solutions that could relieve the stress put on the system. When there weren't enough ventilators for the patients who needed them, they developed prototypes for a computer-controlled ventilator splitter. When surgical gowns became more expensive to use, textile researchers designed a better-fitting surgical gown that simplified manufacture. When a factory-issued part of the full-body PAPR hazard suits kept breaking, a large team came up with a 3-D printed alternative to keep the suits in circulation. ■ ESZ

The Secret Sauce in COVID-19 Vaccines

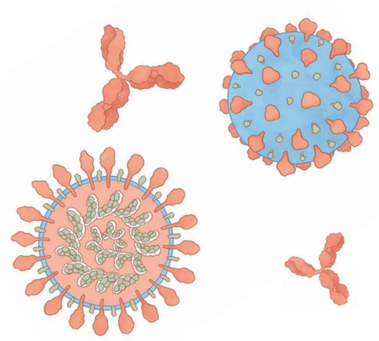
The first two COVID-19 vaccines in the U.S. were a unique formulation: mRNA strands packed inside of a nano-sized layer of fat — a lipid nanoparticle. The mRNA held instructions for making the COVID-19 spike protein, and the nanoparticles offered a convenient way to fuse easily with the lipid covering of our own cells. However, because the vaccine wasn't expected to cause all of the inflammatory side effects — like fever, chills and body aches — that it did, Botond Igyártó, PhD, and team wondered whether the lipid particles might be to blame. To find out, they injected mice with the lipid nanoparticles alone (no mRNA), and saw massive inflammatory reactions. Their work showed that the nanoparticles were not just for mRNA delivery, but also could have been responsible for jump-starting the immune response, and giving some of us those achy post-vaccine symptoms. ■ ESZ

At Home with Dementia during the Pandemic

Isolation, due to COVID-19, became a necessity in the past two years, especially for those 65 and older due to their high mortality risk. But limiting social interaction presents challenges for maintaining mental wellbeing. It is particularly problematic for persons with dementia, as social engagement is often used to slow the progression of dementia. Together with colleagues, Kristin Rising, MD, and Angela Gerolamo, PhD, interviewed patients with dementia and their at-home caregivers about the most challenging aspects of the COVID-19 pandemic. Respondents described how prolonged isolation led to feelings of loneliness, depression and worsening memory problems. Caregivers felt a heightened responsibility and burden for care, and reported often putting their own needs on hold. The work highlights the need for healthcare providers to develop and provide interventions and tools to support families who care for people with dementia. ■ ESZ

Predicting the Severe Cases of COVID-19

One of the most unsettling facts of COVID-19 is how difficult it is to predict when the disease will turn deadly. For some, there are only mild symptoms; for others the disease can turn severe in a rapid and unexpected manner. Colleagues from the Department of Medicine and Department of Surgery built a tool to help clinicians predict those severe cases that would require closer monitoring. Using machine learning and clinical experience, the investigators defined a list of eight predictors that included risk factors such as age, sex, diabetes or labored breathing, together with clinical measurements collected by blood test. They used these input variables to create a web-based tool that could be accessed at the bedside on a phone or tablet. ■ ESZ



BY THE NUMBERS

ABOUT THOMAS JEFFERSON UNIVERSITY

69,500 alumni

1,900+ full- and part-time paid faculty

$1.7 billion endowment

8,200+ students

10 COLLEGES AND **4** SCHOOLS WITH **200+** undergraduate and graduate programs

1,000+ patents for new drugs, software innovations, medical devices & diagnostic tools

RESEARCH FUNDED IN 2021

1,175 active clinical studies ACROSS **THOMAS JEFFERSON UNIVERSITY** and **JEFFERSON HEALTH,** *including...*

48 clinical departments

$87,010,203 in NIH funding

$220,131,494 from funding organizations such as NIH, DOD, HRSA, Genentech and COVID-related funding from the PA Department of Health

300+ clinical research personnel

92.8% increase in NIH funding since 2016

250% increase in team-science grants from NIH over **5** years

60% increase in clinical trials over **5** years

414 externally funded PIs

38 applied research proposals submitted with 18 funded (47% success rate), totaling more than $3 million

Marcella McCoy-Deh, PhD

Inflecting the Narrative on African Studies

Inflection points can be powerful events. They can prompt an individual to take on a new career challenge. And on occasion, that individual's decision can redound to the benefit of thousands of others. Such may be the case for Marcella McCoy-Deh, PhD, associate professor of American Studies and director of the Philadelphia University Honors Institute.

For Dr. McCoy-Deh—an educator, researcher, university administrator and author — her personal inflection point arrived during her time as a Fulbright Scholar at the University of Ghana's Kwame Nkrumah Institute of African Studies (IAS) in 2019-20. She had chosen that institution for both personal and professional reasons: her husband was raised in Ghana, and they were eager for their daughter to have a deep experience of the country and culture. The Nkrumah Institute's faculty is widely respected, including accomplished educators and researchers from across Africa and around the world.

There, she collaborated with faculty to bring relevant material from U.S. history into courses on the slave trade, Pan-Africanism and the African diaspora. She soon found that many assigned readings in courses addressing slavery and colonization in Africa were authored by non-African scholars. It was a telling sign of how knowledge is defined and distributed in the field of African Studies.

"While new perspectives are slowly working their way into textbooks and curriculum, the main body of scholarship about Africa is still rooted in Euro-centric interpretation of events," Dr. McCoy-Deh explains. "Too often, those materials included skewed interpretations, contained omissions or were dominated by European and colonial perspectives."

She had long known about the need to "decolonize" African Studies, but had not understood the depth of the problem—nor its broader effects on African scholars. That realization spurred her to consider—more directly and intently than she had before—how to transform the way scholarship about African culture and history is assessed and presented in global academic literature. Discussions with colleagues such as University of Ghana historian and IAS Research Fellow Dr. Edem Adotey made clear that progress depended on African researchers and educators being able to overcome a fundamental challenge: having their intellectual contributions actually acknowledged, then objectively assessed and validated. "Too often, non-African scholars simply reject or ignore information and ideas that challenge long-held, Euro-centric views," Dr. McCoy-Deh observes.

But there is also a very practical challenge. "While African scholars are conducting high-quality research, too little of their work makes it to broadly accessible journals and textbooks," she adds. And even when their studies are published in journals at African universities, those publications are frequently not accessible on international databases such as JSTOR and Google Scholar.

As a result, a substantial portion of scholarship produced by African researchers is difficult to access, and a generation of comparative scholarship by African researchers is effectively lost to researchers outside of the country or region of origin.

Dr. McCoy-Deh thought deeply about ways to help bridge the access gap, and tested her ideas with colleagues at the Nkrumah Institute. Their discussions gave rise to a collaborative initiative called Africa in First Person. It will be a searchable online repository of work by African scholars writing on the African experience, providing abstracts of unpublished articles and links to published papers. Initially, the repository will invite submissions of material addressing Western academic dominion in African scholarship, as well as articles rejected by scholarly journals for lack of deference to Western ideas.

"Our primary goal is that the repository becomes a widely accessible information resource for editors, researchers and students—in Africa and around the world," Dr. McCoy-Deh says. "Longer term, we hope that Africa in First Person will become a bridge creating new collaborations among researchers and connecting scholars with publishing organizations." A key step in the process is developing the financial support needed to launch the project, and she is currently working to identify potential funders.

As planning for the initiative evolved, Dr. McCoy-Deh realized that her commitment to supporting the work of African scholars had also evolved into a personal and professional inflection point. "Before I went to Ghana, I was uncertain what the next phase of my career would hold. Continue in academic administration? Dive more deeply into my research or writing?" she says. "But I have become passionate about this project, and I am deeply committed to addressing the challenges faced by African scholars."

The broader impact of that commitment could well empower researchers and educators at academic institutions across the continent and help remake the way Africa is studied and taught for generations to come. ■ KM, MM

Manuela Tripepi, PhD

A Journey of Adaptation

Consider Haloferax volcanii, a single celled organism that thrives in extreme conditions such as the very salty Dead Sea. Scientists study it for clues about potential life on Mars and about how organisms may adapt to Earth's changing climate. Much like the organism she studies, *H. volcanii* researcher Manuela Tripepi, PhD, is an expert at adapting to challenging situations.

Dr. Tripepi, assistant professor of Biology, was raised in southern Italy, and following in the footsteps of her father, was drawn to the world of biology. She pursued a PhD in plant biology at the University of Calabria, focusing on how plants respond to stressful environments. But even as she was completing that doctorate, she began to carve out another scientific path. Her thesis work on the salt tolerance of olive plants led her to seek out a researcher on the other side of the world at the University of Pennsylvania — Mecky Pohlschröder, PhD, a widely respected investigator of micro-organisms called haloarchaea, of which *H. volcanii* is an example. Dr. Pohlschröder was deeply impressed by their initial conversation and saw a lot of herself in this young, immigrant researcher. A continuing dialogue ensued, with Dr. Tripepi bringing a plant biologist's perspective to the world of microbiology and spurring a flow of interesting research questions. Dr. Tripepi was invited to work on a summer project in the Pohlschröder lab. Ultimately, she stayed on, simultaneously completing her PhD work on olive plants and foraying into the world of haloarchaea.

The intellectual excitement of that work prompted her to make the audacious decision to pursue a second PhD, in microbiology, which she received from the University of Pennsylvania in 2013. Through that thesis work, Dr. Tripepi was the first to show that — contrary to current dogma — *H. volcanii* is motile and able to move in response to environmental stimuli like light or food. "This work opened up new avenues of research," observes Dr. Pohlschröder. "In fact, I have students in the lab still building on Manuela's foundational work, to understand how motility adds to the adaptation strategies of *H. volcanii*."

Dr. Tripepi joined Jefferson in late 2019 to continue her research on *H. volcanii*, focusing on the effects of sub-optimal temperatures and ultraviolet light on the organism's motility. Just as she was setting up her lab, however, the pandemic hit, forcing her to hit pause. But alongside her bench research, she also does pedagogy-focused research and curriculum development through her role as course director for undergraduate microbiology. For example, she creates laboratory activities that give students first-hand experience with original research projects. She developed a COVID-friendly protocol to monitor wildlife on Jefferson's verdant East Falls' campus — using remotely operated trail cameras placed in different locations, students collected data on patterns in wildlife behavior, including how the pandemic-caused variance in human activity affected the animals' presence. The rich body of student-developed data has been the basis for poster sessions, thesis projects and a new grant-funded expansion of the project to observe birds with smart bird feeders. Dr. Tripepi has also published a description of the protocol so that other institutions can provide a similar undergraduate research opportunity.

Dr. Tripepi's scientific and academic journey of adaptation has been mirrored in her personal life. Her move to the U.S. from Italy was fueled, in part, by her search for acceptance as a member of the LGBTQ+ community. "Coming to the U.S. gave me greater freedom to live my life authentically," she recalls. "I worried less about what people around me would think." Reflecting back on those years, Dr. Pohlschröder says, "Even though things were changing at the time, there were not many openly LGBTQ+ scientists the in academic space. It was very impactful for students and the younger generation of scientists to not only see Manuela accept herself, but accept them too."

While progress has been made, Dr. Tripepi notes disparities and barriers continue to persist for LGBTQ+ scientists. A recent survey showed that LGBTQ+ scientists were more likely than non-LGBTQ+ colleagues to experience harassment and career obstacles; and research has shown that having more visible LGBTQ+ role models in science would make it easier for other LGBTQ+ students to join the field.

"Visibility matters," says Dr. Tripepi. "I share my story with my colleagues and students. Although I am an underrepresented minority in science, I am privileged compared to other communities, and I want to help my students receive the same kind of opportunities I've had." ■ **KM, MM**

A Path Towards Digital Equity

Telemedicine is a vital tool in health care, but it's leaving some patients behind. Jefferson researchers are on a mission to improve 'digital readiness' in under-resourced communities to bridge inequities.

BY **KARUNA MEDA** | ILLUSTRATIONS BY **ERIN K. ROBINSON**

It was the beginning of March 2020, and Chelsea Torres had just returned home to Philadelphia from college for spring break. A few days into her stay, everything changed. Whispers of a deadly pathogen had turned into full-throated cries of caution, and the country went into lockdown. Chelsea and her parents were alarmed when they began to feel unwell — vague symptoms that they probably would have chalked up to a cold in any other circumstance. But amidst the novel coronavirus, they didn't want to take any chances, and hastened to get tested. An agonizing few days of waiting confirmed their suspicions — they had COVID-19. Soon, they began to hear of more cases in their tight-knit Latino community. Many of their family members and friends had underlying health conditions and/or were essential workers and therefore at higher risk of contracting the virus — it was the first glimpse into the disproportionate impact COVID-19 would have on the community. Like many in the diaspora with relatives living abroad, they also grew concerned about their family back in the Dominican Republic.

Over the next few days and weeks, Chelsea and her parents navigated the uncertainties of trying to get care. This meant using telemedicine, which many healthcare centers had transitioned to. Chelsea used her smart phone and computer routinely, and had already adjusted to online learning; using telemedicine didn't daunt her. But her parents weren't as accustomed to technology, and needed her help accessing patient portals and setting up video visits. There was something else that was holding them back that Chelsea couldn't quite put her finger on; it seemed like mistrust and apprehension about this new form of medical care.

A couple of miles away at Jefferson Health, Kristin Rising, MD was noticing something similar.

The Digital Divide Includes Access and 'Readiness'

"It was all hands on deck," recalls Dr. Rising, an emergency medicine physician and clinical researcher.

An onslaught of patients sickened by the coronavirus was quickly filling up the clinic; meanwhile those with chronic illnesses and other health concerns still needed care. Fortunately, Jefferson Health had been honing its telehealth platform — JeffConnect — since its launch in 2015, and was poised to expand the service.

"Our call volumes tripled overnight," says Anna Marie Chang, MD, an emergency medicine physician working closely with Dr. Rising, and a core member of the JeffConnect team. "We trained more than a hundred doctors across the enterprise to handle the influx."

Even as telemedicine sky-rocketed during this first wave of the pandemic, there were many patients who didn't have the resources to access it. A glaring spotlight was put on the 'digital divide' that particularly impacts patients of lower socioeconomic and educational status, communities of color, those who are older, or living in rural areas. These were the same communities that were being hit hardest by the pandemic. Without addressing the lack of access, telemedicine could worsen the impact of COVID-19 and existing health disparities.

As part of the Coronavirus Aid, Relief, and Economic Security (CARES) Act, Jefferson Health received funding from the Federal Communications Commission (FCC) (as well as from the Philadelphia Mayor's Fund, TD Bank, and Aetna/CVS) to expand their telehealth-related services. Dr. Rising led the application of the CARES funds which were used to purchase iPads and remote monitoring devices to give to patients who didn't have devices at home. But she and her colleagues soon realized there was another challenge.

"Enabling access to devices didn't mean patients were automatically going to make a telehealth appointment the next day," she explains. "It was clear that many patients just weren't comfortable using telehealth, and we needed to find out why."

Dr. Rising started delving into research published on 'the digital divide' in an effort to guide solutions. She came across the term 'digital readiness' — it was a concept that encompassed the complexities surrounding the use of technology and addressed three main questions:

1. Does a person have access to a device/technology, and the skills or knowledge to use it?
2. Does a person accept the technology as a relevant tool for its designated purpose, e.g. online learning or telemedicine?
3. Does a person trust the technology?

These questions provided a framework for understanding nuances that drive patient behavior, like those Chelsea observed in her parents.

> **"It's about a mind shift that we as healthcare providers have to help people get through."**
> *Dr. Rising*

"For so long we've thought about the digital divide mainly in terms of access and knowledge," says Dr. Rising. "This concept of 'readiness' shows us that it's more about a mind shift that we as healthcare providers have to help people get through."

Bridging the Digital Divide

It was apparent that patients were on a spectrum of digital readiness, and the critical next step was to identify those who were less 'digitally ready.' At the Sidney Kimmel Cancer Center — Jefferson Health, physicians were alarmed to realize that this was a significant portion of their patient population.

"Cancer patients tend to be older, and many belong to racial and ethnic minorities, a reflection of complex health disparities," explains Brooke Worster, MD, who specializes in palliative medicine for cancer patients. "Many of these patients were less likely to have access to or use technology in their everyday life, let alone in their cancer care. If we didn't reach out to them, they could be in danger of not getting vital treatment, screening and follow-up care."

With astonishing speed, Dr. Worster and colleagues mobilized resources and staff, which included social workers, research assistants, physicians and nurses, and by late March 2020, they had created the Telehealth Taskforce. It was designed to provide one-on-one assistance to cancer patients with smartphone set-up and delivery, creation of email accounts and online health portals, testing device video and audio, and real-time help during telehealth visits. Each patient had different needs, and assistance was tailored accordingly. Because of COVID restrictions, all this had to be done over the phone or a video call.

The Telehealth Taskforce provided a model for how to triage telehealth assistance, and Dr. Rising saw an opportunity to expand it to other areas of care. She collaborated with Rosemary Frasso, PhD from Population Health, and others, to create the Digital Onboarding Taskforce in September 2020. They recruited public health and medical students who were eager to get hands-on patient-care experience and offer help during a time of crisis. They provided similar one-on-one, virtual assistance as the Telehealth Taskforce. Together, the two initiatives helped more than 2,000 Jefferson Health patients overcome barriers to using telemedicine, including access, knowledge and acceptance.

But, Dr. Rising says, there was one component of 'digital readiness' that still lingered— the multi-layered issue of trust.

Mistrust in Health Care Affects 'Digital Readiness'

Before the pandemic, Black patients used telehealth services less often than

"I have an opportunity to help them feel empowered to use resources like telemedicine to take charge of their health."

Chelsea Torres

white patients, but that gap widened substantially as telehealth became the primary way to see a healthcare provider. In the early months of the pandemic, Dr. Rising and geriatric psychiatrist Barry Rovner, MD, led a group of researchers to assess what could be contributing to this disparity. They surveyed 162 Black patients with diabetes and found that despite the fact that over 90% of the participants had the technology and capability to access telehealth, only 39% had a telehealth visit during the pandemic. They looked at contributing factors like age, gender, years of education, cognitive ability—and it had nothing to with any of those. It all came down to trust.

"Participants had less trust in doctors' ability to diagnose and treat their symptoms using telehealth," explains Dr. Rovner. "There was also the fear of discrimination, and that doctors don't always have their best interests at heart."

These fears are justified, given the long history of abuse towards communities of color in the U.S. medical system — from the infamous Tuskegee Study to Henrietta Lacks, a Black woman whose cells were taken from her body without her consent and widely used in medical research. The mistrust is also rooted in a lack of representation in the medical field — less than 6% of doctors in America are Hispanic, only 5% are Black, and less than 1% are Native American. For patients like Chelsea Torres and her parents, it's a struggle to find culturally competent care.

"It shows up in basic things — a doctor might tell me to eat more vegetables and presume I understand that to mean leafy greens, cruciferous vegetables, etc.," explains Chelsea. "But, in Latino culture, vegetables are beans, legumes, plantains, and others that I only know the names for in Spanish. There's a disconnect."

Chelsea also describes how her parents grew up with a very different healthcare culture in the Dominican Republic — home remedies were a staple, like soothing teas made from herbs in the garden; if there was a health concern they would often call the family doctor, or even get advice from the local pharmacist; medications were cheap and didn't require an appointment to refill.

"If you're used to low-cost, low-effort health care, it can be really overwhelming to navigate the U.S. medical system," says Chelsea. "Then there's the added concern about being discriminated against, dismissed or not understood. And now you're being asked to use this new thing called telemedicine? It's just one more barrier. I understand why my parents are apprehensive."

Engaging Communities to Build Trust

It became clear to Dr. Rising that in order for telehealth to be truly inclusive, building trust in under-resourced communities would be instrumental in sustainably leveling the playing field of 'digital readiness.'

"But trust is not something you can build overnight," says Amy Leader, PhD, a key collaborator of Dr. Rising and public health researcher who studies health disparities. "There are deep, systemic, generational issues at play, and it's going to take a lot of work to dismantle them."

"The taskforces reiterated a key tenet of my research — listen to patients," says Dr. Rising. "This is the first step to building trust, and it means adopting a high-touch approach: get into the communities and start conversations."

Community-led organizations are a conduit to those conversations and the lived experience of navigating health care. Esperanza Health Center, a multi-cultural ministry providing holistic health care to the Latino and under-resourced communities of Philadelphia, is one such example. Esperanza has been instrumental in providing access to culturally competent, multi-lingual care all through the pandemic. And their leadership observed similar limitations in telehealth engagement as Dr. Rising did. A natural partnership formed in the winter of 2020, with the eventual goal of developing a toolkit to improve digital readiness in Latino populations in the Greater Philadelphia area. The toolkit would include educational materials, in readily understandable language and in Spanish, to address telehealth-related barriers specific to this community. Eventually, this 'digital readiness' toolkit will be replicated in other communities; Dr. Rising hopes to do so through an emergent telehealth advisory board that includes partners such as Philadelphia Fight, Philadelphia Chinatown Development Corporation and SEAMAAC (Southeast Asian Mutual Assistance Association Coalition). Together they serve refugee, immigrant, and other under-resourced populations across Philadelphia.

In order to understand the specific drivers of mistrust of telehealth in the Latino community, Dr. Rising and Esperanza leaders are currently conducting interviews and focus groups with community members, led by a trusted liaison. Chelsea Torres is one of them. She had interned at Esperanza three years ago, and had returned to volunteer during the pandemic, providing education about the vaccines and helping schedule appointments. She heard about the project with Jefferson Health and was chosen to be a community research assistant. In this role, she will collect and digest qualitative data from her interviews with the community, which will in turn inform the development of the toolkit. It's a responsibility that she takes very seriously.

"I come from a big family, and many of my loved ones struggle with health conditions that maybe went neglected because they couldn't find culturally competent care," Chelsea says. "As someone they trust, I have an opportunity to help them feel empowered to use resources like telemedicine to take charge of their health."

"It's critical to have Chelsea on our team, and the focus groups are a key element of the process of building relationships with communities that have felt disenfranchised for so long," says Dr. Rising. "As researchers and healthcare providers, we need to demonstrate that we're invested in listening and making changes based on what communities are telling us."

Connecting Efforts for Sustainable Change

Translating the lessons learned into action is what drives the Center of Connected Care, which launched in January 2021 with Dr. Rising at the helm. Behind her is a multidisciplinary team, the core of which is formed by Drs. Worster, Leader and Chang — they bring a range of expertise and perspectives, from social work and population health to nursing, cancer care and emergency medicine. One of their foundational missions is to ensure digital equity across all communities. This means equitable access, comfort, trust and flexibility of care.

"Health care is not 'one-size-fits-all' and there will always be patients who prefer in-person care to telehealth," says Dr. Rising. "But the idea is to give everyone the ability to include telemedicine in their healthcare toolbox, and the confidence to use it when they want to."

The partnership with Esperanza, which is in its nascent stages, is an example of the unique patient-centric approach

"This is the first step to building trust, and it means adopting a high-touch approach: get into the com-munities and start conversations."

Dr. Rising

the Center will take in addressing digital readiness and their overall goal of tackling health disparities. It reflects a shift in the field, from research *on* the community, to research *with* the community, say Drs. Leader and Rising, whose collaborative and independent work have often included a community or patient-advisory board. "That's where trust comes from, when it feels like you're part of the solution," says Dr. Leader.

The Center will also expand on the lessons learned from the taskforce; one in particular is the need to measure the range of digital readiness in the patient population. Dr. Worster says that if they had identified the least digitally ready patients ahead of time, there would have been a safety net for them when the pandemic hit and forced the shift to telemedicine. The Center hopes to provide that by integrating a 'digital readiness' screening questionnaire into patient care. The idea would be to administer it when patients first interact with the health system, whether through telemedicine or during an in-person visit. It would then be administered annually thereafter to capture how digital readiness may change with ever-evolving technology, says Dr. Chang. The data collected from these assessments will help design evidence-based and targeted interventions.

For example, if trust is the biggest barrier for a specific patient group, then an intervention would be centered on having educational and information-gathering sessions with trusted and culturally competent liaisons. Similarly, in an upcoming grant, Dr. Leader and Dr. Rising propose embedding a team of specially-trained patient navigators dedicated to telehealth into clinical settings to guide patients who are less comfortable with technology.

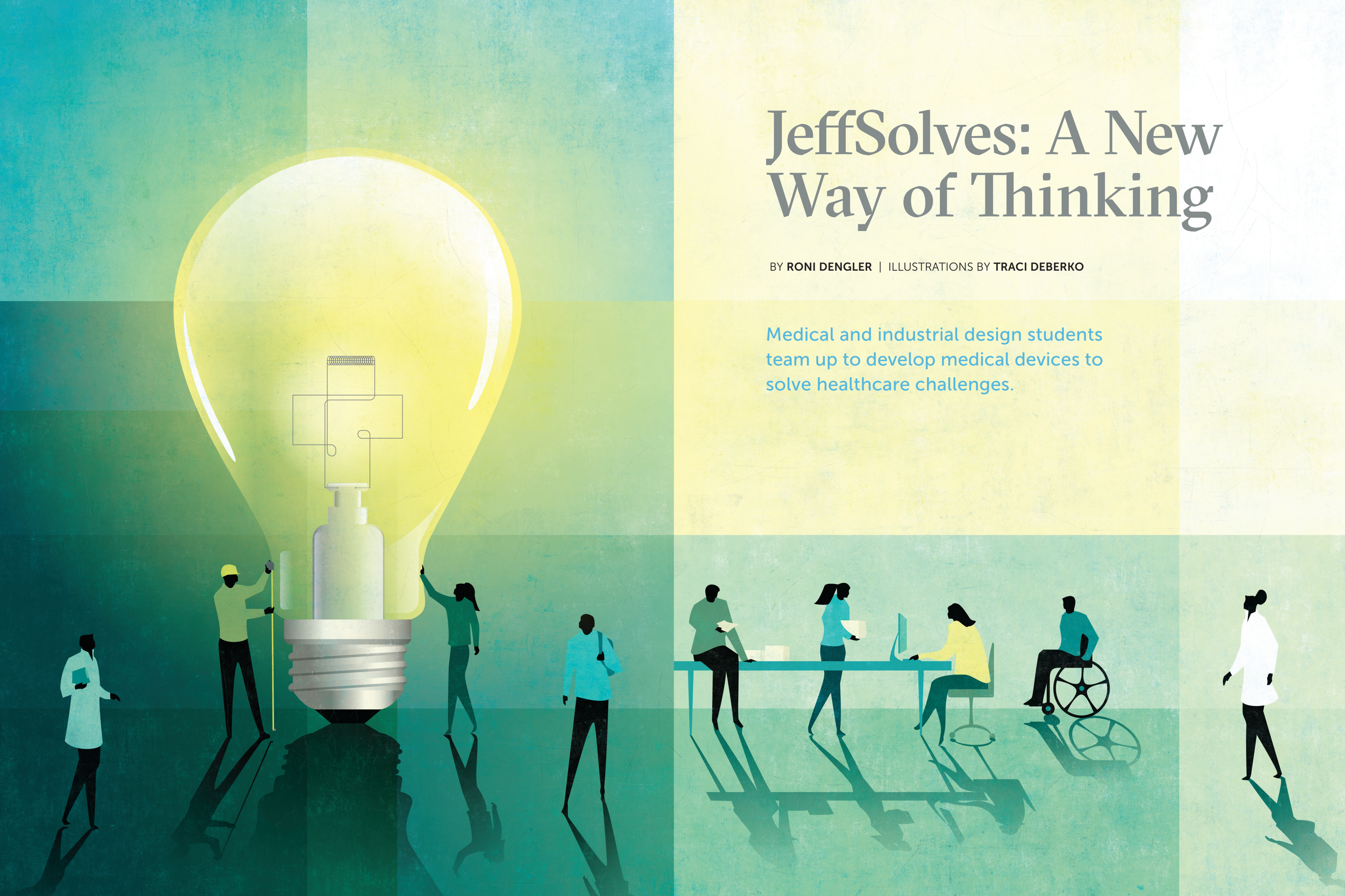
The team has a long road ahead of them, but Dr. Rising is excited about convincing funders and policy makers to invest in digital equity. A sign of their progress already — they will host a national conference funded by PCORI (the Patient Centered Outcomes Research Institute) in spring 2022, bringing together diverse stakeholders from across the country who have been tackling digital readiness in their own communities to determine best practices, understand knowledge gaps and develop new research partnerships.

"It took a pandemic to bring telemedicine and digital inequities into razor-sharp focus," says Dr. Rising. "And telemedicine is here to stay, so it's up to us to ensure that it becomes a means of decreasing health disparities, and not increasing them." ■

JeffSolves: A New Way of Thinking

BY **RONI DENGLER** | ILLUSTRATIONS BY **TRACI DEBERKO**

Medical and industrial design students team up to develop medical devices to solve healthcare challenges.



Design isn't what most aspiring doctors think about when considering medical school. But for Emily Marshall, a second-year medical student, design drew her in when interviewing to attend Sidney Kimmel Medical College at Thomas Jefferson University.

Through the JeffSolves MedTech program, Jefferson offers medical students like Marshall a rare opportunity to design and develop a novel medical device from the ground up.

"People who go into medicine don't have exposure to designing medical devices, even though we're using them every day," Marshall says. "The JeffSolves program is a very unique opportunity to learn about what goes into product development in the medical space."

Now entering its seventh year, JeffSolves teams medical students up with industrial design students to identify a real-world healthcare challenge that a medical device could solve.

The student-teams work with clinicians, patients and experts in engineering and design to conceptualize and develop a medical product. The process includes giving products a name, creating a brand and submitting provisional patents on the products to protect the intellectual property.

This year, 19 students who broke into four product-designing groups worked on their project over the course of six months, plus full-time over the summer. In addition to guidance from Industrial Design and Health Design Lab faculty, JeffSolves partnered for its third year with Bresslergroup, a local design firm that specializes in medical devices. Teams also worked with Savvy Cooperative, an organization where patients are compensated for their expert knowledge about their conditions. The new partnership helped to provide teams with patient insight and to foster patient-centered designs.

The program culminates in public disclosure of the student-teams' ideas to seek interested parties that might help move the product forward, with the ultimate goal of selling the intellectual property to a medical device company to manufacture the product. Students from this year's program presented their products to a combined in-person and virtual audience as part of Design-Philadelphia, an annual 10-day festival that highlights the city's impressive design community.

"The idea of the program is to empower students," says Rob Pugliese, PharmD, director of innovation design and co-founder and managing director of Jefferson's Health Design Lab, out of which the JeffSolves program runs.

Conpono Collar

Marshall had first heard about JeffSolves from a former participant before she enrolled at the medical school, and the program intrigued her. But when the time came to come up with a project, she and her team struggled to zero in on a problem to address. In prior years, the JeffSolves program started with a reverse pitch night," where clinicians and physicians would lay out a smorgasbord of problems for the student teams to solve with their products. This past year, however, identifying key health problems to solve was up to the students. They had to identify problems that they felt strongly about and believed had market viability within this year's program theme: neurology, neuroscience and rehabilitation.

Marshall and her group, mentored by Morgan Hutchinson, MD, director of education for the Health Design Lab, went to the experts. They met with Jefferson neurologist Hristelina Ilieva, MD, PhD, who specializes in amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disease more commonly known as Lou Gehrig's disease. The conversation revealed that patients with ALS and other neuromuscular conditions wear cervical support collars to help weakened neck muscles support the head.

Jennifer Hegelein (left) and Emily Marshall (right)

In talking with patients, Marshall and her teammates realized that the current spectrum of available cervical collars on the market weren't meeting patient needs. Collars were either intense medical-grade collars intended for immobilizing the neck to prevent spinal cord injury, or over-the-counter collars that did not provide sufficient support. One patient explained how difficult it is to eat with a collar on. "That stood out to us," Marshall says. "The device should permit patients to do the things they still can do at this point in their disease, because eventually those things are taken away from them."

Drawing on patient input, the team aimed to create a collar that is not only sturdy enough to provide sufficient head support for patients, but also flexible enough that they can eat and do other routine activities while wearing the collar. To achieve this, Marshall and her teammates designed a collar with a pivoting jaw piece. They started by hacking apart existing collars and trying to re-configure them to include an adjustable and movable mechanism.

But the design truly came together when they discovered a mechanism on helmets that welders use to protect their eyes and faces from ultraviolet light and sparks when heating metals. Welding helmets have a part that rotates the helmet into different height settings. Marshall and her team took this mechanism out of a welding helmet and put it into one of the handful of prototype collars they made, "and it works pretty well," she says.

Throughout the design process, the team tested their prototypes on themselves to find out what was and wasn't working. The group is now working on refining the model and will soon move to a 3D printed version before testing with patients.

"It's a very different way of thinking about diseases than we do in typical medical education," says Marshall. "Going forward, I want to make sure I always ask questions about a patient's needs and issues with medical devices."

Emily Marshall (medical student), Jennifer Hegelein (industrial design graduate student), Nia Robinson (industrial design undergraduate student), Eshika Agarwal (medical student)

Grip'N'Go

With a background in biomedical engineering, second-year medical student Sara Belko found that the JeffSolves program was a natural fit.

"I want to be that link between medicine and engineering, because right now there's a big gap," she says. "Engineers are making products that don't necessarily solve patients' problems, and doctors are taking these products and actually modifying them to be better."

Belko and her team decided to focus on spinal cord injury and interviewed patients who use assistive devices like wheelchairs, walkers and canes to find out what issues come up for them in their everyday lives. A topic that kept cropping up was sanitation concerns around using public restrooms.

To use the toilet, people who use wheelchairs often have to grab the toilet seat with their hands to transfer their bodies from the chair to the toilet. The lack of sanitation hinders people from wanting to use public toilets. Also, toilet seats aren't very sturdy. People who use wheelchairs don't feel very stable when transferring from their chair to the toilet. Some have even fallen while transferring because the seat snapped. Wheelchair-accessible stalls with bars aren't always available or in the right position.

To design their product, the team started by understanding what the transfer from wheelchair to toilet seat looks like. Guided by teammate Aaron Anderson, who uses a wheelchair, they broke down the process into 28 different steps. The team went into public restrooms to observe different versions of the environment they were working in. Then they went a step further. They bought and installed a toilet and set up a mock environment so they could practice transfers themselves and better understand a user's perspective.

Belko and her teammates, mentored by Kristy Shine, MD, PhD, assistant professor of Emergency Medicine and director of Scholarly Inquiry at Sidney Kimmel Medical College, went through many iterations of concept design and testing, 3D printing more than a dozen prototypes. After testing on 30 toilet seats, the team produced Grip'N Go, a portable weight-bearing handle that attaches to the

Left to right: Blake Rivas, Aaron Anderson, Hannah Anderson, Emily Furstenberg, Sara Belko present their device at the pitch event at the Bresslergroup which took place on October 13, 2021.

toilet to enhance stability and sanitation. With the device, no bigger than a purse, users no longer have to touch the toilet seat during self-transfer. Belko and team are now moving forward with two designs and hope to test them with patients who use wheelchairs soon.

The project helped Belko embrace areas of medicine and life that often feel taboo to speak about. "No one really likes to talk about how private toileting is," Belko says. "All the patients we talked to were super appreciative that someone was finally talking about these issues."

Sara Belko (medical student), Aaron Anderson (industrial design graduate student), Emily Furstenberg (medical student), Hannah Anderson (medical student), Linda "Blake" Rivas (medical student)

Soleia

Industrial design student Gigi Geary participated in JeffSolves in 2020 with a team that developed a flexible barrier to minimize contamination in IV lines, a device called Conexo. This year, Geary and her new teammates chose to work on cerebral palsy, a condition that affects movement, balance and posture. It is often the result of abnormal brain development before birth. Many individuals with cerebral palsy who are able to walk do so with an altered gait.

The team, mentored by Bon Ku, MD, assistant dean for Health and Design and director of the Health Design Lab, met with doctors, physical and occupational therapists and patients to learn more. Patients noted that their shoes would wear down very quickly. Online support groups revealed that many patients require shoe lifts because one leg is significantly shorter than the other. Shoe lifts can be expensive and often must be special-ordered from a shoe company. Because children grow so fast, kids with cerebral palsy are often limited to one pair of shoes, which doesn't always match their attire or the occasion.

Team Soleia's goal is to make walking more comfortable for pediatric patients with leg-length discrepancies, and to increase the longevity and adjustability of shoe lifts. Using some of their old shoes, the team met up over the summer to try out different design ideas and materials. "Sometimes it felt like carpentry," says Katie Bormes, a medical student on the team. "We were in the design lab using a band saw to cut out shoe shapes from foam."

To test out their design ideas, Bormes, Geary and their teammates would attach prototypes to their old shoes, then walk, run and jump while wearing them. There were multiple rounds of tweaking the design. Bormes says the iterative design process provided a new way of thinking, compared to the step-by-step problem solving and diagnosis in medical school.

To address patient concerns with current shoe lifts, the group's designs are sleek, either incorporating design elements of patients' existing shoes, or creating lifts in neutral colors that blend in rather than stand out.

Left to right: Anusha Koka, Zane Gouda, Kathryn Bormes.

Ideally, the team would like the shoe to adjust over three shoe sizes and be interchangeable between pairs of shoes. They're working on refining the attachment mechanism. Given that their target patient population struggles with maintaining balance, they want to be certain that their product is highly stable for everyday activities. Once they are confident in the safety, the team will send it out for user feedback to continue to improve the design.

"It's going to go far and help so many people, and at the end of the day, that's what I want to do as a designer," Geary says.

Gigi Geary (industrial design graduate student), Katie Bormes (medical student), Jane Won (industrial design undergraduate student), Anusha Koka (medical student), Zane Gouda (medical student)

TremEase

Medical student Jenna Mandel and her teammates decided to develop a customizable weighted glove for patients with benign essential tremor, a neurodegenerative disorder that is personal to Mandel. Her grandmother has the condition. Benign essential tremor causes involuntary, rhythmic shaking that is often most prominent in the hands. Movement exacerbates the tremor. There are limited treatment options, and, for many patients, the available treatments only work for a short period.

Left to right: Jenna Mendel, Joey Paladino, Kayla Brockmeyer demonstrate the TremEase gloves.

It can be an isolating disease. Patients' hands shake when bringing food or a drink to their mouths, which causes spills, leading to embarrassing and frustrating experiences for patients that can deter them from going out in public. Over time, tremors get worse.

When Mandel and her team joined online support groups for people with essential tremor, they asked members about their biggest day-to-day problems. Then working with Savvy Cooperative, they conducted video interviews with patients. This intensive, patient-centered approach revealed a gap in currently available weighted gloves that help to dampen tremors. On one end of the spectrum, there are one-size-fits-all gloves that are cheap but do not work very well. On the other end, there are gloves that are tailored to an individual's specific tremor and work much better, but are very expensive, with poor insurance coverage. Moreover, each individual's tremor is unique, requiring personalized design elements in their gloves.

"We started to ask ourselves if we could create something cost-effective that could be tailored to each patient's tremor," says Mandel.

The team put together 50 prototype drawings and produced a handful of physical prototypes. Using a breathable material, the team designed anti-tremor weighted gloves that have a Velcro-like material on the backside, where small weights can be attached to any part of the glove, as more intense tremors tend to require more weight to dampen. "We wanted to make it as low-profile and as comfortable as we possibly could," Mandel says. They are easy to put on, pull off and wash, and moving or adding weights is simple.

Mandel and her teammates were able to test the glove with a few patients. At the DesignPhiladelphia event, Mandel and her team, who were also mentored by Dr. Ku, showed a video demonstration of a patient using the glove. Without the glove, the individual's hand shook visibly while performing an everyday work task; *with* the glove, his movements were fluid and without tremor. "It was powerful to be able to demonstrate the benefit of the gloves for actual patients," says Mandel.

Jenna Mandel (medical student), Justin Horst (industrial design graduate student), Fletcher Viders (medical student), Joseph Paladino (medical student), Kayla Brockmeyer (medical student)

Future Forward

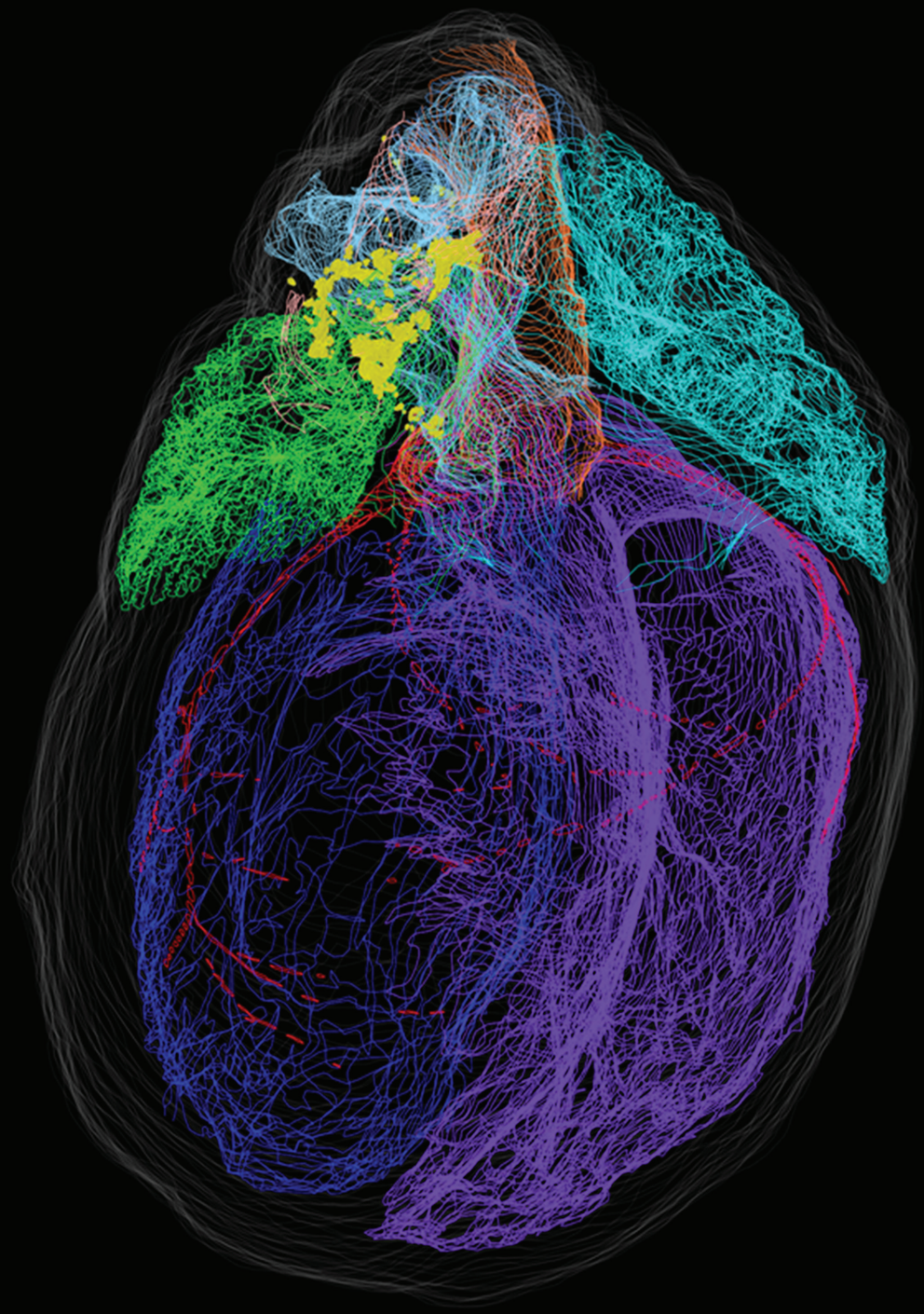
The teams from this year's JeffSolves MedTech Challenge program are now refining designs and testing them on patients in the clinic.

Mandel and the TremEase team are currently in the process of applying for Institutional Review Board (IRB) approval, which will enable the team to assess the utility and validity of TremEase on patients in the clinic. In the meantime, they continue to modify the design based on user feedback. Ultimately, they hope to make TremEase available as an over-the-counter product or through an online provider, such as Amazon, as soon as possible.

Similarly, Sara Belko and her teammates are in the process of applying for IRB approval to test out different handle designs for the Grip'N Go and to see how patients will use it long-term. The team has submitted a provisional utility patent and is advertising the device on a UK-based digital partnering platform called IN-PART that connects university research with industry R&D, where they hope to match with licensing opportunities.

Marshall and her teammates are further refining a few design details before developing a computer-assisted design and 3D-printing the Conpono collars to test with patients in the ALS clinic at Jefferson, for example. Soleia is on a similar path.

"By connecting students with clinicians and patients, and empowering them to work with the engineers and designers who can give them the tools to solve problems by creating a product, JeffSolves operates much like a start-up," Pugliese says. "All these devices have promising futures." ■



The Heart's "Little Brain"

Researchers develop the first ever 3D map of the heart's nervous system, providing a foundation for understanding the complexities of heart health.

BY **KARUNA MEDA**

On the computer screen, a 3D model of a heart rotates seemingly in mid-air, a carousel of colors and contours. Amidst the blue and purple waves that denote the heart's powerful muscles sit a cluster of yellow dots. To anyone else, it looks like a meaningless blob. But to James Schwaber, PhD, and Raj Vadigepalli, PhD, it represents a culmination of nearly three decades of work, a long-awaited key to a world of unanswered questions.

Let's rewind...

"The map demonstrates that the local control of the heart is much more nuanced than we've been able to appreciate..."

Dr. Vadigepalli

Thirty years ago, the scientific and medical communities were desperately trying to find answers for heart disease, which has been the single biggest killer in the United States since 1921. Attention turned to a massive and meandering network of nerves called the vagus nerve — it carries signals from the brain, the master organ of our body, to other organs, including the heart. Scientists found that when these signals weren't sent properly, it could actually impair heart health and even lead to heart failure. When they poked the vagus nerve with an electrode to help jump start it, they found that an ailing heart could actually pump better! It was a thrilling finding. But there was a problem: the scientists didn't know where the vagus nerves ended in the heart — was it a certain chamber, or a muscle, or an electrical node? Which of these connections could explain how the vagus nerve affects heart health?

Around the same time, the early 1990's, researchers found that the heart had nerve cells or neurons that were akin to the ones that made up the brain. In other words, the heart had its very own nervous system that could function independently of the brain! Affectionately called "the little brain" of the heart, it became a point of fascination in the field — why does the heart need its own nervous system anyway? How does it help the heart function? It also became a potential target for the vagus nerve. Could a connection between the brain and the "little brain" be the key to restoring heart health?

Drs. Schwaber and Vadigepalli have been at the forefront of trying to answer these questions for the last 25 years, giving critical insight into the heart's nervous system. In the last five years, serendipity brought them together with like-minded experts and advanced technology that allowed a major breakthrough: the first-ever 3D map of the heart's "little brain." It is a map that gives an unprecedented look at not only how the neurons are organized in the heart — that undiscerning blob of yellow dots — but also their biological properties. For the first time, our researchers are able to appreciate the spatial *and* functional relevance of the heart's neurons in keeping the organ healthy, giving us new clues about how to tackle the longstanding issue of heart disease.

Tracing the Connections between the Heart and the Brain

The connection between the heart and the brain goes back to 1884, when the psychologist William James famously described this scenario: "Imagine you are walking through the woods, and you come across a grizzly bear. Your heart begins to race. You feel afraid, and you run." The concept suggests that the physical reaction (a racing heart) drives the emotional experience (fear). This interplay has always fascinated Dr. Schwaber.

In the early 1990's, he was at the DuPont Company in Wilmington, Delaware, and was particularly interested in the burning question at the time — how does the vagus nerve connect to the heart?

By then, researchers discovered that the vagus nerve connected to the sinoatrial node, which controls heart rate. "That connection made sense for heart health," says Dr. Schwaber. "But I wanted to know if the vagus nerve connects to the ventricles, the chambers that pump blood to the rest of the body. A connection here could be beneficial too."

To shed light on this, Dr. Schwaber turned to a molecular biologist at DuPont by the name of Lynn Enquist, PhD, who was developing a novel technique using a modified virus to label multiple relay points in a neural pathway. When Drs. Schwaber and Enquist injected the virus into the ventricles of the rat heart, they traced the connections all the way back to the neurons in the brain that gave rise to the vagus nerve. They had just shown that the vagus nerve does indeed connect directly to the ventricles!

It was a major finding that challenged the accepted view on how the vagus nerve might affect the heart. But there was push-back — some believed that the observation was simply an artifact of the new tracing technique. The field needed convincing with more conventional methods.

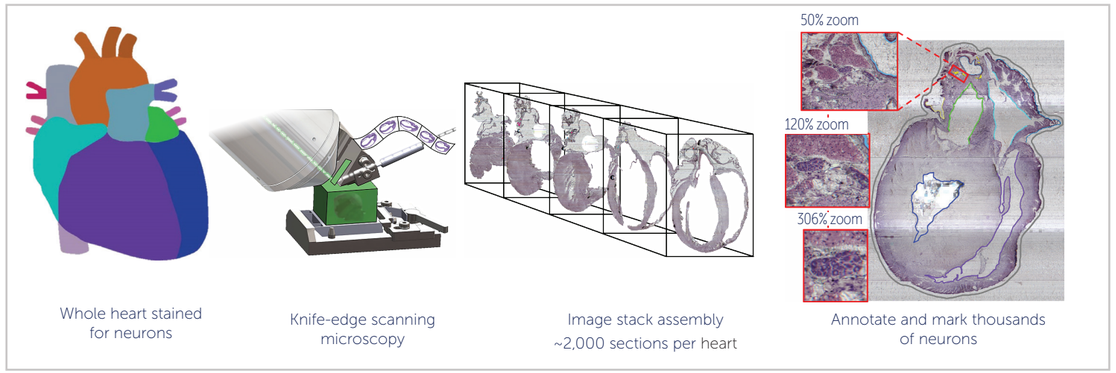
Dr. Schwaber had help from a former lab member — Frank Doyle, PhD — who had just started his first faculty position in chemical engineering at Purdue University and recruited a postdoctoral researcher, Zixi Cheng, PhD. They were able to validate the earlier findings, but their tracing revealed something else — as nerve fibers left the heart to go the brain, some looped back into the heart. In fact, they were going back to the heart's "little brain," which had just been described in 1991 by a scientist named Dr. J. Andrew Armour. It was still poorly understood, and the researchers were unsure what to make of this internal loop. This is where Dr. Vadigepalli entered the scene.

The Heart's "Little Brain" through the Eyes of an Engineer

Dr. Vadigepalli was pursuing his PhD in systems engineering at Purdue University in Dr. Doyle's lab when he was pitched this idea of a new circuit between the brain and the heart.

Male vs. Female: *A comparison of the "little brain" in the male heart (yellow dots) and female heart (pink dots). The distribution of the neurons is different, and there are fewer neurons in the female heart.*

Images captured by ***Shaina Robbins, MS***



How to build a 3D heart: *The fully digitized, single-cell resolution images were painstakingly made by slicing a heart stained for neurons, and then mapping those labeled-image sections onto a computational scaffold.*

"...the heart's 'little brain' resembled an internal loop that engineers call local controllers — so what is this one adding to the control of the heart?"

Dr. Vadigepalli

"The last time I took a biology class was in high school," says Dr. Vadigepalli. "I didn't know anything about all the controversy that surrounded this new anatomy – but it was fascinating to me from an engineering perspective."

The heart reminded Dr. Vadigepalli of a control system, a bread-and-butter concept of engineering. Control systems are all around us – think about the cruise control in your car that maintains a safe speed, or the thermostat that works to keep your home at a preferred temperature. These systems work in such a way that when you change the information input, they can adjust to achieve the desired outcome.

"The heart receives input from the brain about our internal state and environment, and it adjusts to maintains outputs like heart rate, blood pressure, etc. accordingly," explains Dr. Vadigepalli. "But the nerve fibers that were found going back into the heart's 'little brain' resembled an internal loop that engineers call local controllers – so what is this one adding to the control of the heart?"

This became the basis of Dr. Vadigepalli's thesis work, from the mid to late 1990's. Through mathematical modeling, he found that when the internal loop was on, it could fine tune how the heart responds to signals from the brain. This improved the heart's performance and made outputs like heart rate more reliable. When it was off, the heart's "little brain" couldn't correct local disturbances, and the external loop to the brain had to be recruited instead, making the control system less efficient. Without the internal loop playing this role of damage control, the heart could become erratic, leading to an irregular heartbeat or arrhythmia – or so the modeling predicted.

This work finally shed some light on the function of the heart's "little brain" and provided evidence for it to be an ideal target for the vagus nerve. It also gave rise to new opportunities for integrating systems engineering into the field. But these mathematical models were hypothetical, and needed to be proven with experimental work. Many questions remained.

A SPARC of Serendipity

In 2000, Dr. Schwaber and Dr. Vadigepalli brought their respective expertise to Jefferson, joining forces in the new Daniel Baugh Institute for functional genomics and computational biology, which Dr. Schwaber led.

For the next decade, they switched focus from the heart to the brain, studying the "central controller." Scientists had developed maps of the brain in different animal models that could pinpoint the position of individual neurons and the genes they expressed. These maps gave insight into how neurons could be spatially organized in intricate circuits, and how their genetic identity determines their function in these circuits. It was exactly the kind of map they needed for the heart, says Dr. Vadigepalli, to help them understand the function of the "little brain." But such a map did not exist yet.

In 2015, their luck began to change when a NIH funding program called 'Stimulating Peripheral Activity to Relieve Conditions' or SPARC was conceived. It brought together researchers who studied different organ systems and their communication with the brain, a concept called interoception. The interplay regulates vital bodily functions like digestion and breathing, but can also influence our mood and cognition. Much of the field of interoception has focused on the vagus nerve, which in addition to heart health, can affect the health of the liver, the gut, the lungs, etc. The ultimate goal of SPARC is to develop therapeutic devices that can change electrical activity in nerves, like the vagus, to treat conditions like heart failure, inflammatory disorders, diabetes, and more.

"SPARC filled this massive void in the field and reignited our interest in the 'little brain'," says Dr. Schwaber. "But there was so much more we needed to understand about its anatomy and function."

As they revisited their old stomping grounds in the heart, serendipity struck again. They came across two new technologies — one, an automated imaging technique that could precisely reconstruct any tissue in 3D; the second, a software that could build manipulable images and videos of these 3D reconstructions. Both companies were shopping for customers. It was a match made in scientific heaven.

Drs. Schwaber and Vadigepalli recruited a core team of trainees between their two labs — Sirisha Achanta, lab manager at the Institute, Alison Moss, a graduate student, Jonathan Gorky, a MD/PhD student, Shaina Robbins, a research assistant — and went about building a methodological protocol from scratch. They brought their old colleague, Dr. Cheng, now at the University of Central Florida, back into the fold as well, along with his graduate student Clara Leung.

By 2019 the team had created a dual approach pipeline — one using the imaging technologies to build a precise 3D reconstruction of the entire rat heart viewable via computer screen; and the other using a technique called laser capture microdissection to sample single neurons for gene expression analysis. This allowed them, for the first time ever, to build a 3D map of the heart's "little brain" in the rat — one that showed the individual positions of the neurons within the heart's anatomy, as well as their genetic properties.

A Map to Endless Possibilities

As the researchers behold the floating 3D heart on the computer screen, each turn illuminates new questions about the cluster of yellow dots that represent the "little brain" — how are the neurons organized around key structures of the heart? Can this influence how hard and fast the heart pumps? How do the neurons communicate with each other, and with signals from the brain? Does this organization and communication change in heart disease? Given that heart physiology differs between males and females, does the "little brain" differ between sexes?

The 3D map has revealed some of these answers, amidst hitherto unknown complexity of the heart's "little brain." The researchers found that the neurons in the rat heart are clustered around the sinoatrial node, positioning them optimally to monitor and regulate heartbeat. The map also allowed them to pinpoint how the "little brain" is organized and wired differently in male vs. female rats; for instance, although they found fewer neurons in the female heart compared to males, it doesn't impact the heart's essential functions. This provides clues as to why there may be differences in cardiovascular disease between men and women.

The team also explored the "little brain" in the pig heart, which is more anatomically comparable to the human heart. They found that unlike neurons of the brain, which are often defined by the chemical they release — either ones that augment or depress activity, etc. — neurons of the heart had much more fluid expression of these chemicals. It was as if the heart's neurons contained multiple identities. The various permutations and combinations allow the neurons in the "little brain" to fine tune how the heart responds to signals from the brain. This validates Dr. Vadigepalli's thesis work, which demonstrated this fine-tuning in mathematical models.

"The map demonstrates that the local control of the heart is much more nuanced than we've been able to appreciate," says Dr. Vadigepalli. "It suggests that a single drug that turns heartbeats up or down, may not be as effective as one that hits the right combination of targets. There is much more to explore in developing new therapies for heart disease."

The researchers are currently using the map to understand how the vagus nerve connects to the neurons of the "little brain" and provide highly anticipated evidence for how the vagus affects heart health. They hope their findings, and work from their SPARC colleagues, will also provide the physiological underpinnings for how mental states (e.g. stress), and interventions that alter them (e.g. meditation), affect the whole body.

"We've created a foundation for developing 3D maps for other organs in animal models and, ultimately, in humans, in health and disease," says Dr. Schwaber. "These maps are the key to the brain-body connection. The possibilities are endless." ■

"We've created a foundation for developing 3D maps for other organs in animal models and ultimately in humans, in health and disease. The possibilities are endless."

Dr. Schwaber

RNA Like You've Never Seen Before

New methods to 'see' unstudied types of RNA reveal an incredibly abundant regulatory molecule that plays a role in disease and health alike.

BY **EDYTA ZIELINSKA** | ILLUSTRATION BY **MONIKA JASNAUSKAITE**

The human genome project, a race to map out the code of human life, was supposed to uncover untold secrets of human health and disease. But even before the 15-year project was finished, researchers began to realize that there was much more to understanding life than the string of genes that coded for proteins. How did the cell decide how much of each gene to produce, and when? It became clear that knowing when to turn specific genes on or off could mean the difference between health and diseases like cancer, Alzheimer's and many others.

In the 1990s, researchers discovered microRNAs, very short sequences (about 22 nucleotides) that came from the region of DNA in between protein-coding genes. These tiny molecules, researchers soon found, were master regulators, fine-tuning the cell's genetic production. The work opened a new field looking at the cell's RNA-regulators, all sped by a tool called RNA-seq that could rapidly detect and decode these novel microRNAs.

That tool, however, was limited to detecting RNA types with a specific, but common, sequence on their tails. In the past few years, Yohei Kirino, PhD, and colleagues developed a new set of tools and modified old ones in order to detect the previously un-seeable world of small RNAs. These tools have revealed the properties of these RNAs, where they come from and how they may regulate health and disease.

A number of these new RNA molecules are fragments of other well-known RNA species, such as ribosomal RNA, messenger RNA and transfer RNA, and contain a cyclic phosphate (cP) tag at their end — a different "tail" than microRNAs. Researchers had known of these fragments, but assumed they were simply junk — chopped up pieces meant for the cell's recycler.

In 2015 and '16, Dr. Kirino's lab published the method to detect these cP-containing RNAs (cP-RNAs). It was simple enough: add a processing step to remove the cP tag from cP-RNAs, before running the usual RNA-seq. With this tool that they called cP-RNA-seq, the researchers began to see just how active these molecules really were.

The cP-RNAs, they showed, were involved in hormone-dependent cancers like breast and prostate cancers. Derived from transfer RNAs (tRNAs), which normally deliver building blocks to a growing protein chain, these cP-RNAs were plentiful, especially in hormone-driven cancers, and appeared to promote cell replication, a key driver of cancer growth.

Dr. Kirino and colleagues went on to find other types of cP-RNA involved in unrelated diseases, from neurodegeneration to infection. During infection with tuberculosis, for example, the researchers found cP-RNA present at 1,000 times the concentration as in healthy individuals. What's more, these cP-RNAs appeared to act as a cytokine, spreading the alarm for inflammation and immune activation. Unlike cytokines, which are a chemical signal, the cP-RNA would jump across membranes within an exosome bubble released from one cell and absorbed by another. Once inside, they activate a toll-like receptor,TLR-7, that detects and responds to RNA molecules and activates immune cells.

Most recently, the group discovered that cP-RNAs were involved in helping maintain genome integrity in sperm and egg cells. They showed that cP-RNAs are the precursors to piRNA, a familiar and essential molecule that silences jumping genes — transposable elements — in these germline cells. This silencing prevents jumping genes from introducing mutations that can cause harm or even kill the cell.

"The Computational Medicine Center is developing methods, computational and experimental, for identifying different classes of RNA and determining their function. Dr. Kirino's work uncovered an intriguing class of RNA that had remained 'invisible' to standard sequencing approaches," says Isidore Rigoutsos, PhD, Richard W. Hevner Professor and Director of the Computational Medicine Center.

The Kirino group developed other tools to see the unseen RNA world. They created the YAMAT-seq, an efficient method for sequencing tRNA, and the four-leaf clover qRT-PCR to quantify these twisted molecules; and the Dumbbell-PCR, a method to quantify specific variants of microRNA and other small RNAs.

New RNA Toolkit

cP-RNA Seq
cP-RNA-type decoding

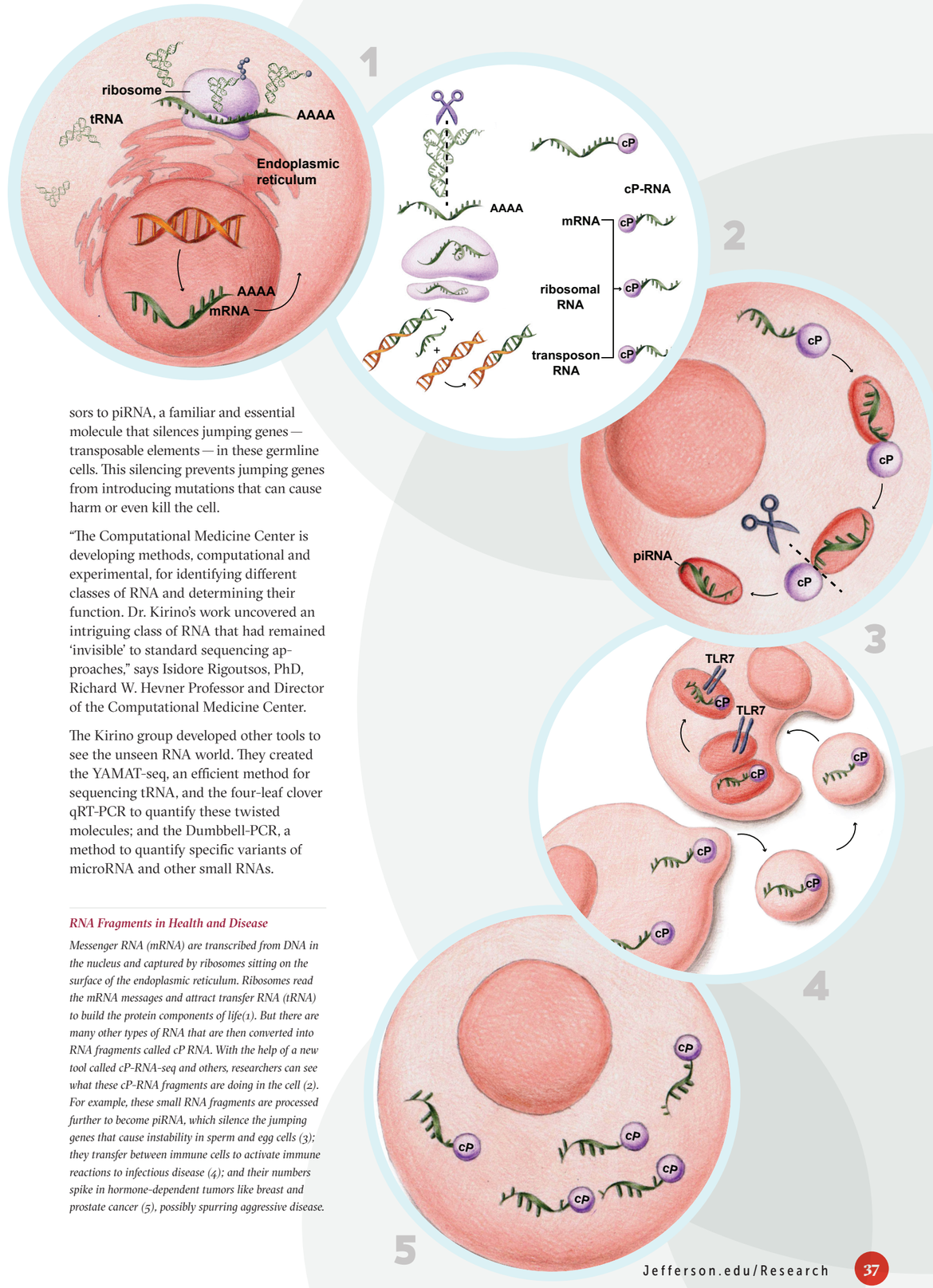
YAMAT Seq
Rapid tRNA decoding

4-Leaf Clover PCR
Rapid tRNA counting

Dumbell PCR
Rapid counting of RNA variants

RNA Fragments in Health and Disease

Messenger RNA (mRNA) are transcribed from DNA in the nucleus and captured by ribosomes sitting on the surface of the endoplasmic reticulum. Ribosomes read the mRNA messages and attract transfer RNA (tRNA) to build the protein components of life(1). But there are many other types of RNA that are then converted into RNA fragments called cP RNA. With the help of a new tool called cP-RNA-seq and others, researchers can see what these cP-RNA fragments are doing in the cell (2). For example, these small RNA fragments are processed further to become piRNA, which silence the jumping genes that cause instability in sperm and egg cells (3); they transfer between immune cells to activate immune reactions to infectious disease (4); and their numbers spike in hormone-dependent tumors like breast and prostate cancer (5), possibly spurring aggressive disease.



ONLINE CONTENT

Explore our visual and interactive stories.

Video: *Mind Over Matter*

One stroke patient's journey as he helps test if brain implants and a robotic arm brace can restore physical abilities.

Twitter Infographics: Mid-Career Invisibility

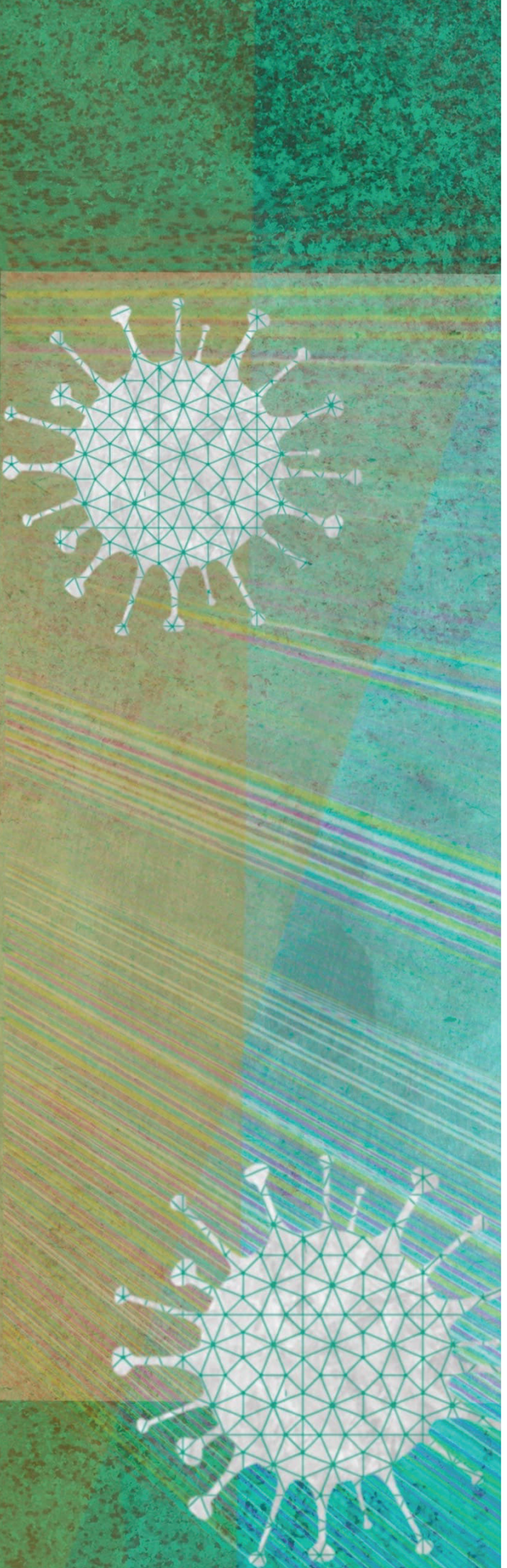
The micro and macro inequities that drive career stagnation of women in academic medicine.

Animated Illustration: To Sleep or Not to Sleep

How male fruit flies decide whether to sleep or mate.

Black History Month Twitter Series

Jefferson highlights Black excellence in our research community through our twitter spotlight series.



ARCHITECTURE

BUSINESS

DESIGN

ENGINEERING

FASHION & TEXTILES

HEALTH

MEDICINE

SCIENCE

SOCIAL SCIENCE

Jefferson

Thomas Jefferson University

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

Jefferson.edu/Research