Thomas Jefferson University

RESEARCH

CONVERGENT THINKING, CREATIVE APPLICATION

inside

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ABOUT THOMAS JEFFERSON UNIVERSITY

8,200+
students

2,600+
faculty
(full- and part-time paid)

69,500
alumni

160+ graduate and undergraduate programs across **10** colleges and **4** schools

$941 million
endowment

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

"Jefferson's research portfolio has almost doubled in the past 10 years. And our investment in both people and technical infrastructure will drive continuing growth in the Jefferson research enterprise's size and its achievements."

Brian N. Squilla, MBA
Chief Research Officer

RESEARCH FUNDED IN 2020

1,112
active studies across Thomas Jefferson University and Jefferson Health, including 33 clinical departments

245
clinical research personnel

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

$84,592,376
in NIH funding–an approximate **38%** increase since 2016

60% increase in clinical trials over 5 years

384
externally funded Principal Investigators

$166,280,122
from funding organizations such as National Institutes of Health (NIH), the U.S. Department of Defense, the Health Resources and Services Administration, the Pennsylvania Department of Health, Genentech Inc. and BriaCell Therapeutics Corporation

21 clinical trials focusing on treatment of COVID-19 and over **260** Jefferson publications about COVID-19 since March 2020, spanning topics including basic virology, clinical research, healthcare implications and societal impact

A Note About Our Research Centers and Institutes

One way we accomplish our distinctive programmatic approach to research is by organizing as multidisciplinary centers and institutes around specific challenges. Led by visionaries and staffed by experts, these entities enable us to more quickly move discovery to translation and application; and they are excellent environments for training colleagues and students to address the practical challenges the world presents. There are dozens of these institutes and centers within Jefferson; here we list just a few of them. Many of the faculty members highlighted in this publication are affiliated with one or more of these research engines—powerhouses of discovery such as:

Fashion and Textiles Futures Center—where faculty and students conduct research and engage in industry-sponsored real-world projects with partners including NASA, Under Armour and Target, and focused on market changes, sustainability and interdisciplinary collaboration.

Institute for Smart and Healthy Cities—an aggregator and facilitator of transdisciplinary research and education driving the future of our cities and communities and focusing on transforming urban environments into more efficient, healthier and livable cities.

Jane & Leonard Korman Respiratory Institute–Jefferson Health and National Jewish Health—where world-class researchers pursue bold new avenues of study on lung development and respiratory diseases; focusing, for example, on genetic determinants of airways disease, pulmonary fibrosis, pulmonary hypertension, lung inflammation and tobacco-related disorders.

The NCI-designated **Sidney Kimmel Cancer Center at Thomas Jefferson University**—which has been an international leader in oncology research, patient treatment and patient education for more than 25 years. The Center's research program includes cancer cell biology and signaling, molecular biology and genetics—focusing on a broad range of malignancies, including prostate cancer, gastrointestinal cancer and brain tumors.

Vickie and Jack Farber Institute for Neuroscience—where globally recognized researchers and physicians from neurosurgery, neurology, psychiatry and neuroscience collaborate on advancements in treating neurological injury and neurodegenerative disorders, including conditions such as Parkinson's disease, epilepsy, ALS, MS, stroke, and spinal cord and traumatic brain injury.

"Jefferson has always had world-class researchers. But the strategy we have pursued over the past decade has spurred a unique convergence of expertise, intellect, creativity and resources—one that has substantially increased our collective impact. The growth of our team-science portfolio, for example, has been nothing less than spectacular, and its future is bright."

Steven B. McMahon, PhD
Senior Associate Provost for Programmatic Science
Professor and Chair, Biochemistry and Molecular Biology

For more information on Jefferson's Research Centers and Institutes, please visit:
Jefferson.edu/Research

Convergent Thinking, Creative Application

> **...We are amassing an ever-growing understanding of nature's genius—the exquisitely adapted molecular and genetic machinery cells used to accomplish a multitude of purposes. I believe we are on the brink of a convergence revolution, where engineers and physical scientists are recognizing how we can use this biological 'parts list' to adapt these natural machines to our own uses."**
>
> –Susan Hockfield, PhD, MIT president emerita, neuroscientist and author

Dr. Susan Hockfield's exciting and hopeful book, *The Age of Living Machines*, describes how researchers have worked across disciplines and fields to engineer biologically based solutions for complex problems. These solutions—examples of which range from cancer-detecting nanoparticles and mind-reading bionic limbs to virus-built batteries, protein-based water filters and computer-engineered crops—grow from "convergence," the integration of knowledge from the life and physical sciences and engineering. And Dr. Hockfield eloquently makes the case that convergent thinking offers humanity's best chance to overcome the globe's most vexing challenges.

At Jefferson, we share that sense of the power inherent in convergence. We believe there is a kind of energy created when once-distinct disciplines intersect: the light of the resulting discovery is extraordinary, as is the warmth of human benefit from applying that discovery. For that reason, we continue working hard to bring people, ideas and resources together in new ways—creating opportunities to apply knowledge, methods and technologies from one field, to questions asked in another.

Research 2021 offers a glimpse of how convergent thinking is manifest across our institution. You can see it, for example, in the multidisciplinary team testing the first brain implants designed to help stroke victims regain limb function; and in the novel solutions developed to address the challenges of caring for COVID-19 patients. Convergent thinking is evident in the ways that our faculty and student researchers are combining research from architecture, industrial design and occupational therapy to develop plans for smart, healthy cities. It is evident too in our hemp industry research and development program, in which faculty and graduate students are using new knowledge about

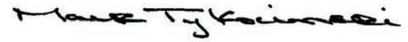
business systems, policy making, materials science, manufacturing processes and design to lay the foundation for a robust and sustainable new industry.

In addition to its importance in developing solutions, I would argue that convergent thinking can be key to teasing apart the interwoven problems that comprise complex challenges—and to gaining a more nuanced understanding of the interplay between seemingly unrelated causes. The work that researchers across the University are doing to understand disparities in cancer treatment outcomes is an important example. So too is our exploration of psychological and cultural influences affecting caregivers' unrecognized biases about sexual assault victims and patients from underprivileged backgrounds. And our society's lack of convergent thinking on racial issues is the driver for Jefferson faculty research on the inequitable ways that minority communities and journalists are treated by mainstream news media.

Reading *Research 2021* makes clear the extraordinary level of knowledge, skill, creativity and dedication displayed by our faculty, research staff and students. What may not be as clear is the deep institutional commitment that underpins their work: Jefferson continues to invest in the people, systems, technologies and space necessary to advance the University's research enterprise. We are committed to building on areas of strength; to fostering collaboration across research fields and professional disciplines; and to creating an environment highly conducive to discovery, translation and application of new knowledge.

We are determined to provide our researchers the most advanced technical resources possible. The University's new Cryo-Electron Microscopy system, for example, will open new paths of discovery in biomedical science, and will create opportunities for research and development in materials science, textile engineering and physics. And while less technologically sophisticated, our digital research support systems—such as LabArchives, our state-of-the-art, cloud-based electronic research notebook—have been hailed as pioneering ways of fostering a collaborative and efficiently managed research ecosystem throughout the institution.

Jefferson's expanding technical resources and research infrastructure go hand-in-hand with our sustained growth in funding. Our strong commitment to providing internal funding for preliminary studies and pilot grants has been a driver for substantial expansion of overall funding: Over the past five years, the University's external funding for research has more than doubled, and the number of clinical trials undertaken has increased approximately 60 percent.



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

The Jefferson research enterprise is robust and growing. We are having major impact across the research spectrum—from making fundamental discoveries on the nanoscale and atomic levels to the translation and application of new therapies, processes and products in health care, industry, local communities and multifaceted ecosystems.

As the past year made clear, the world relies on dynamic, dedicated and practically focused research institutions like Thomas Jefferson University to drive forward the discovery and application of knowledge. Indeed, rarely in history has there been a similar convergence of unbounded opportunity and fundamental challenge as we have today. Or such an imperative for bridging boundaries—intellectual, professional, economic, political and cultural—as we strive to answer the questions being asked of us in the 21st century.

I invite you to read on and discover the many ways that Jefferson researchers are moving past old boundaries to pursue opportunity and surmount our world's most significant challenges. ■

Striving to Understand Disparities in Cancer Care

A key element of the mission of the Sidney Kimmel Cancer Center–Jefferson Health—and an objective of many researchers across the University—is to understand and mitigate the disparities in cancer incidence, treatment and outcome too often experienced by patients who are African American or Latinx, have low incomes or have limited access to care.

In the Philadelphia region, for example, prostate cancer incidence and mortality rates are significantly higher for African Americans than Caucasians, but the causes of this major disparity are unknown. Many researchers have believed that the difference in outcomes results from African American men's poor clinical response to existing treatment for advanced disease, as compared to Caucasian men's response. But a groundbreaking study—led by **William Kevin Kelly, DO**, professor of medical oncology and urology—directly challenges that long-held concept.

"Indeed, the study is paradigm shifting," observes **Karen E. Knudsen, MBA, PhD**, CEO of the American Cancer Society, former enterprise director of the NCI-designated Sidney Kimmel Cancer Center.

Dr. Kelly's study was a meta-analysis of patient data from 8,820 men with metastatic castration-resistant prostate cancer (mCRPC) who had been treated with a docetaxel and prednisone (DP)-based regimen during nine phase III clinical trials. The group included men who self-identified as either Caucasian, Black or Asian (with four percent not specifying). The primary goal of the analysis was to compare the response to therapy and overall survival.

The results: "We observed no differences in clinical outcomes by race and ethnic groups," says Dr. Kelly. "And, in this case, 'no difference' is a highly significant finding. The fact that Black, Asian and Caucasian men who were treated the same did equally well in the clinical trials strongly suggests that there are other causes for the poorer outcomes and mortality rates experienced by Black men with mCRPC."

This study was one of a series that Dr. Kelly and his colleagues are conducting on treatments and other factors that may underpin disparities. "Our ultimate goal is to help pinpoint the drivers of prostate cancer disparities—in particular, whether they are biologically based or result from differences in factors such as quality of care, access to care, or social determinates of health—and identify ways to eliminate them," Dr. Kelly says.

Although the use of a relatively new, effective and less-expensive breast cancer treatment is on the rise, African American women and those without private insurance are too frequently not offered the therapy. As part of a comprehensive treatment plan, the approach—called hypofractionated whole breast radiation (HR)—delivers a higher radiation dose per treatment than the traditional regimen, and cuts the number of treatment sessions roughly in half. The HR approach is as effective as the traditional approach at reducing the risk of the cancer returning for most women. It is also more cost-effective and offers many patients fewer side effects and better breast restoration outcomes following treatment.

Unfortunately, in a study of nearly 260,000 early-stage breast cancer patients, **Alliric Willis, MD, MSPH**, professor of surgery and vice chair and assistant dean for faculty affairs, and research colleagues found that patients who identified as Caucasian were most likely to receive HR, while those who identified as African American were least likely. "Taking all other factors into account, African American women were 15 percent less likely to be treated with HR than Caucasian women," he says. "Thus, even though treatment guidelines do not take race into account, it is clearly a factor in delivery of this often-preferred breast cancer treatment."

Socioeconomic status also apparently affects the delivery of HR therapy: patients with private insurance were more likely to receive HR than were uninsured patients or those on Medicaid; and those who lived in the highest-income zip codes were much more likely to undergo HR than patients from lowest-income zip codes. As well, treatment facilities associated with academic medical centers were twice as likely to use HR as community cancer or integrated network cancer facilities.

"Patients should have access to all treatment options no matter their race, socioeconomic background or where they seek care," Dr. Willis says. "We hope that our research will help to address gaps in provider education and extend this favorable treatment to all patients."

Lung cancer treatment is another area where racial disparities persist—in both outcomes and treatment types. For example, although African American patients are now more likely than they were a decade ago to receive the most-effective treatment for early-stage non-small cell lung cancer, they continue to be less likely than Caucasian patients to receive that treatment. Surgical removal of a portion of lung is the most-effective current treatment; and two types of radiation therapy are used as a second-line therapy, with stereotactic ablative radiotherapy shown to be more effective than external beam radiation therapy for early-stage disease.

> **"We must keep working to reduce barriers to successful treatments for Black patients across cancer types, and better understanding drivers of these inequities is key to fixing them."**
>
> Olugbenga Okusanya, MD

Assistant professor of surgery **Olugbenga Okusanya, MD**, and research colleagues examined information on 192,415 patients in the National Cancer Database to try to understand whether reliance on second-line treatments for African American patients has contributed to the disparities in long-term outcomes across populations.

"We found some progress being made in closing the disparity in the utilization of surgery in Black patients," says Dr. Okusanya, "and no disparity across racial groups in use of the two second-line therapies. Additionally, while other studies have suggested that comorbidities in Black patients were one of the drivers for worse outcomes—rather than the lower utilization of surgery—our research found that when Black patients get surgery there is actually a trend for them to have better survival than their white counterparts."

Dr. Okusanya's studies on disparities in cancer care continue. "We must keep working to reduce barriers to successful treatments for Black patients across cancer types," he says, "and better understanding drivers of these inequities is key to fixing them." ■

Cryo-EM at Jefferson: Driving a New Era of Scientific Discovery

Scientific discovery is often the product of a delicate dance between intellectual insight and technological capabilities. It is a synergistic cycle of advancement where the desire to test a research hypothesis may motivate the creation of a new technology, and the new technical capacity yields unanticipated opportunities for wider discovery. And one of the most important drivers of new knowledge is the development of technologies for viewing biology's fundamental building blocks: the atoms and molecules that comprise living cells.

Since late 2020, Jefferson researchers have been using one of the most powerful devices for "seeing" molecular structures at the atomic level: Cryo-Electron Microscopy (Cryo-EM). The development of Cryo-EM reflects the convergence of technological skill and biomedical purpose. And at Jefferson the device will create opportunities across a broad spectrum—from basic biology discovery research to applications in materials science and textile engineering.

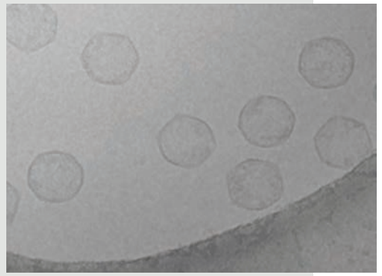
"For many years, X-ray crystallography has been the predominant technique for studying the three-dimensional structure of biological macromolecules in detail," says **Gino Cingolani, PhD**, professor and vice chair of biochemistry and molecular biology and director of Jefferson's X-ray crystallography facility. "But it has limitations: crystallizing macromolecules is arduous and time-consuming; many proteins won't crystallize and the process can alter the structure, misrepresenting the molecule's folding."

Being able to move beyond those limitations is one of the reasons why Dr. Cingolani is so pleased to be guiding the University's newly established Cryo-EM facility. Cryo-EM has become the state-of-the-art technology for describing biological complexes and their mechanisms at their most basic level," he explains. "It enables researchers to generate three-dimensional images of biomolecules, see how they function and how they interact with each other."

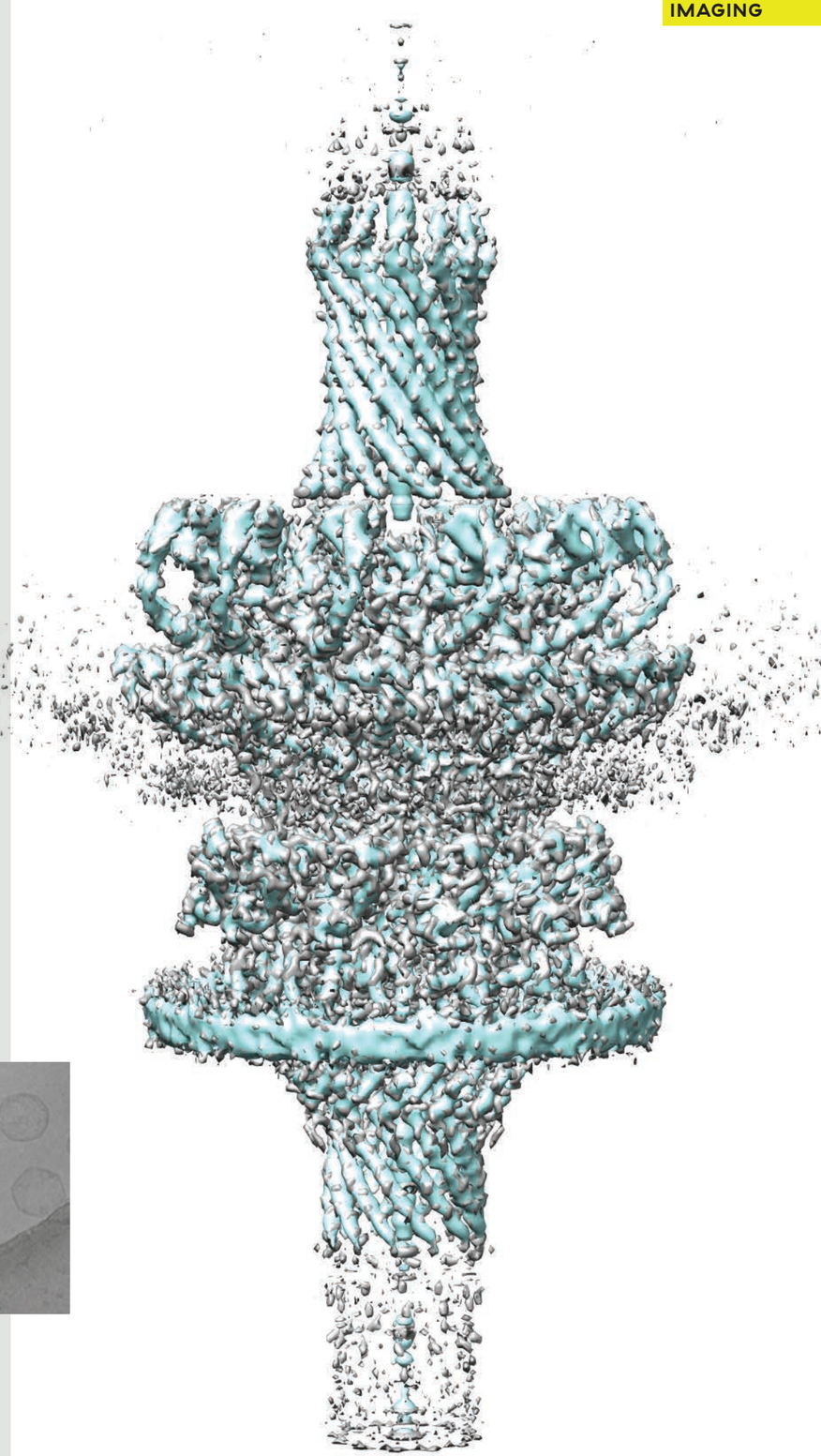
In awarding the 2017 Nobel Prize in Chemistry to the developers of Cryo-EM, the Nobel Committee said, "This technology has taken biochemistry into a new era." In fact, we are benefiting from that "new era" right now. "The mRNA-based COVID-19 vaccines created by the Pfizer-BioNTec, Moderna and others are premised on an understanding of the novel coronavirus's chemical structure," Dr. Cingolani points out. "It was Cryo-EM that enabled scientists to define that structure in just weeks, rather than the years it would have taken using X-ray crystallography."

> **"Cryo-EM enables researchers to generate three-dimensional images of biomolecules, see how they function and how they interact with each other."**
>
> Gino Cingolani, PhD

Jefferson is one of fewer than a dozen research centers in the eastern United States with a dedicated Cryo-EM facility. "This groundbreaking technology is opening exciting new research opportunities across the University," Dr. Cingolani says. "It will vastly expand our ability to understand the mechanisms driving disease at the cellular, molecular, and atomic levels. And it will be a catalyst for development of targeted, highly effective new treatments for a wide range of diseases." ■



The Cryo-EM device captures thousands of two-dimensional images, such as the image ABOVE. It uses computer algorithms to integrate them into three-dimensional visual models of individual and complex molecules, like the image on the RIGHT.



Probing Molecular Mechanisms of Viral–Host Interactions

Zika virus. Atomic level structure, determined by Cryo-EM.

Holly Ramage, PhD, assistant professor of microbiology and immunology, is taking on some of the world's most prevalent infectious diseases. She seeks to understand the molecular mechanisms of viral-host interactions in the flaviviruses — including dengue, Zika and West Nile virus — that are endemic in many areas of the world.

"Increasing evidence indicates that many viruses, including flaviviruses, have evolved mechanisms to manipulate cellular machinery in order to promote infection," Dr. Ramage says. "My lab examines the physical interactions that occur between flavivirus and host-cell proteins. We use powerful proteomics and genomics techniques — including siRNA knockdowns, CRISPR knockouts and mutagenesis strategies — to identify the changes in cellular proteins that allow viral infection and permit viruses to evade the immune system."

Currently, there are no specific antiviral treatments for any of the flaviviruses that infect hundreds of millions of people each year. But scientists do know that in order to replicate, flavivirus proteins must physically engage with — and subvert — a host cell's antiviral capacities. For that reason, Dr. Ramage has undertaken an NIH-funded study that aims to identify the physical interactions that occur during West Nile virus infection and that enable the virus to evade the immune system. In previous work, she pinpointed the cellular proteins that are targeted by West Nile virus in the infection process — and identified that eight of those proteins are also involved in the infection processes used by dengue and Zika viruses. The current study focuses the role that two of those proteins play in antiviral signaling.

"There is strong reason to believe that multiple flaviviruses have a shared mechanism for evading the immune system," Dr. Ramage notes. "Therefore, this work and our follow-up studies may inform new targets for therapeutic intervention against a number of these infections."

Over the past year, Dr. Ramage has also been applying her lab's expertise and approaches to identify drugs that have the potential to stop the SARS-CoV-2 virus in its tracks. The project's focus is the sigma-1 receptor protein, which plays a multifunctional role in scaffolding intracellular membranes and which may be key to how viruses move into and through a cell. This study is exploring the potential to use a specific small-molecule compound that targets the sigma-1 receptor—a compound originally designed to treat prostate cancer—to stop the coronavirus from entering and replicating within cells.

"Coronaviruses are entirely dependent on the host's cellular machinery to replicate," Dr. Ramage notes. "We hypothesize that the sigma-1 receptor could be an important cellular factor that is required by SARS-CoV-2 to replicate and produce new infectious viral particles."

Specifically, this study focuses on the ability of sigma-1-targeted compounds to disrupt two proteins crucial to infection and replication: the virus's spike protein and the host cellular protein TMPRSS2—elevated levels of which dramatically increase susceptibility to SARS-CoV-2 infection in certain cell types.

> **"We hypothesize that the sigma-1 receptor could be an important cellular factor that is required by SARS-CoV-2 to replicate and produce new infectious viral particles."**
>
> Holly Ramage, PhD

"If our central hypothesis is accurate, these sigma-1-targeted agents will block the maturation of the spike protein and suppress cellular TMPRSS2 expression," Dr. Ramage explains, "effectively inhibiting infection." Moreover, they could form the basis for treatments of a range of coronaviruses. ■

Applied Solutions for Pandemic-Spurred Problems

As a university with a large, comprehensive healthcare system, Jefferson has been on the front lines of the pandemic. The situation has required that everyone become a creative problem solver: faculty, staff and students have stepped up to analyze problems as they emerge and develop solutions for an array of issues. It has been a high-pressure demonstration of applied research and development in real time, and a potent example of how the University is spurring a convergence of disciplinary perspectives to address new and evolving challenges.

"Applied science uses in-depth inquiry to rigorously analyze problems and then develop and test answers," says **Ron Kander, PhD**, associate provost of applied science. "Our researchers, students and designers worked hard to understand how COVID-19 changed our work and our lives, and have come up with innovative solutions to overcome these obstacles."

Here are examples of innovations developed to address pandemic-driven challenges.

A Smart Ventilator Splitter

From the pandemic's outset, the nation's too-limited supply of mechanical respirators became a critical concern. These machines typically helped individual patients move filtered air into and out of their lungs—with each device serving one patient at a time. That prompted bioengineer and visiting professor **Alessandro Napoli, PhD**, and **Mijail Serruya, MD, PhD**, assistant professor of neurology, to develop a device that would permit each respirator to serve three patients simultaneously. Their computer-controlled three-way "ventilator splitter" had a digital control panel that would monitor and control the airflow parameters of each patient's lungs; and the lines in and out of the machines had filters for each patient's separate airflow.

Rethinking Surgical Gown Design

Standard surgical gowns do not fully address problems caused by airborne viruses. For example, a widely used type of plastic gown effectively repels fluids; but the tie closure in the back leaves workers feeling exposed. On the other hand, the alternative nylon gown has full front-and-back coverage but is not as water repellant—and is more expensive. Responding to caregivers' requirements, **Anne Hand**, associate professor of fashion design, developed a prototype for a new gown that combined the best qualities of the existing versions. Her gown model provided better full-body coverage and functionality, and could be made with a lockstitch sewing machine, simplifying production and reducing cost.

Negative-Pressure Masks for Oral Procedures

During the pandemic, oral, dental and nasal surgeries can present infection risks to surgical staff performing the procedure. Therefore, a team led by **James Evans, MD**, professor of neurological surgery and otolaryngology, developed a patient-worn mask that uses negative airway pressure to safely exhaust air exhaled by the patient during the procedure. The respirator mask fits snugly around a patient's face, but has a specially designed opening that allows caregivers to pass instruments through.

Bridging Isolation

Patients' social and physical isolation is one of the unfortunate side-effects of the pandemic. Recognizing the importance of human connection during a crisis, an interdisciplinary team of faculty and students undertook the JeffersonSCREEN project: developing a novel physical screen/intervention that enables "mask-less visual connections" between patients and their caregivers, family and visitors. "The product that has been designed and is now being prototyped reflects the knowledge and skills of the unique collection of professional disciplines in our university," observes **Michael J. Leonard, MAEd, MSEd**, dean of the School of Design and Engineering. "We've brought textile designers and textile engineers, industrial designers and architects together to address practical challenges defined by an array of clinicians and caregivers." ■

A COVID-19 Vaccine with Few Logistical Hurdles

One of the challenges posed by the first COVID-19 vaccines to be approved for wide-scale use is logistical: the RNA-based Pfizer and Moderna vaccines require deep-freeze storage and must be used within a relatively short period after they are manufactured. That is a particular problem for less-developed nations and for populations remote from ultra-cold storage facilities.

Researchers at the Jefferson Vaccine Center are working to overcome those and other logistical challenges by leveraging one of their previously developed vaccines. Their COVID-19 vaccine candidate, CORAVAX™—which will soon enter Phase I/II clinical trials—can undergo long-term shelf storage at 4 degrees Celsius, and its freeze-drying formulation has been used with a similar vaccine for Ebola virus.

The vaccine's development was led by **Matthias Schnell, PhD,** Jefferson Vaccine Center director and professor and chair of microbiology and immunology. "CORAVAX™ incorporates a portion of the SARS-CoV-2 spike protein into a 'carrier' formula—a killed-rabies vaccine—that has already been demonstrated to be safe and effective," Dr. Schnell explains. "At least 20 manufacturing facilities around the world are already producing 100 million doses of that vaccine annually—and we'd simply be adding one small component to the formulation.

Because the underlying vaccine is already being widely manufactured, CORAVAX™ could be quickly produced and distributed to serve global needs. "In addition," Dr. Schnell adds, "the production process is relatively low-cost, which will be an important factor where billions of doses may be needed." The Jefferson Vaccine Center is also working on a new version of CORAVAX™ for the emerging Delta variant of SARS-CoV-2.

COVID's Impact on Cancer Diagnosis

While there are studies underway to characterize the direct effects of the COVID-19 pandemic on the care of patients with cancer, there have been relatively few quantitative reports of the impact that efforts to control the pandemic have had on the normal course of cancer diagnosis and treatment encounters. However, a multi-center research team led by **Jack London, PhD**, research professor emeritus of cancer biology, and **Christopher McNair, PhD,** associate director for data science at Sidney Kimmel Cancer Center and assistant professor of cancer biology, is studying that now. They have used encounter data from 20 healthcare institutions to compare numbers of cancer-related patient encounters in early 2019 to those occurring between January and April 2020, as COVID-19 became a pandemic.

The study considered a variety of patient cohorts including: those with existing cancer; those with new incidence of disease; those with specific types of cancer; and those simply undergoing screenings. "We found a significant decline in numbers of patient encounters in the early-COVID period, across the groups studied," says Dr. McNair, "notably including those with new incidence of cancer." Of the cancer types analyzed, lung, colorectal and hematologic cancer cohorts exhibited decreases in patient encounters roughly averaging 39 percent—while decreases for breast cancer, prostate cancer and melanoma ranged from almost 48 percent to nearly 52 percent. In addition, cancer screenings declined drastically, with breast and colorectal cancer screenings dropping by well over 80 percent.

"The steep decreases in cancer screening, and patients with new incidences of cancer suggest the possibility of a notable increase in patients with later-stage cancer being seen initially in the future," Dr. London says. "We also can expect an increased demand for cancer screening procedures as delayed tests are rescheduled." The researchers are currently analyzing the most recent available data from an expanded network of institutions and are working to understand the continuing effects of the pandemic on cancer diagnosis and treatment encounters. ■

Fast-Paced, Frontline Research

While the clinicians of Jefferson Health were on the front lines of the battle with COVID-19—treating nearly 16,000 COVID patients and testing 35,000+ people—just behind them were the basic science researchers working hard to understand the molecular and cellular mechanisms driving the disease and the clinician-scientists working to adapt existing therapeutics to the unique challenges created by SARS-CoV-2.

Since early 2020, Jefferson researchers published more than 260 research studies on the coronavirus's biology and on treatments for severe COVID-19. They have also initiated 21 clinical trials focusing on treatments for the disease's most significant effects.

> **"It took just two weeks to open our study of an intranasal spray with the potential to reduce inflammation in the part of the lungs responsible for air exchange."**
>
> David Whellan, MD

Many of those clinical trials were undertaken with breathtaking speed. "Our clinical research teams worked incredibly hard to get these trials to patients in record time," says **David Whellan, MD,** senior associate provost of clinical research and founder of the Jefferson Clinical Research Institute. "Typically, it takes up to 90 days to finalize regulatory and contracting requirements. But we were able to drive that time way down. For example, it took just two weeks to open our study of an intranasal spray with the potential to reduce inflammation in the part of the lungs responsible for air exchange." ■

Letrell Crittenden, PhD
Assistant Professor of Communication

Racism in the Media

Always tell both sides of a story—that's the old journalism axiom. But, too often, that approach gives equal standing to facts and unsupported claims, and that false equivalence creates public confusion about complex issues ranging from climate change to economic inequality to health care. "More than that, there is evidence that blind insistence to 'both-sides' reporting can invalidate marginalized voices, reinforce racist stereotypes and contribute to structural racism in the media," says **Letrell Crittenden, PhD**, assistant professor of communication.

False equivalence in reporting is just one of the challenges Dr. Crittenden explores in his research on how news organizations report about issues affecting communities of color—and how those organizations struggle with diversity in their own newsrooms. He studies situations such as that experienced by *Pittsburgh Post-Gazette* reporter Alexis Johnson, who was pulled from covering the George Floyd protests in early 2020 because she was viewed as "not objective." Experiences such as Johnson's, Dr. Crittenden says, rob journalists of color of their perspective on issues related to race: "These situations send the message that Black journalists should not offer their knowledge and perspective, even when it's needed most."

At the same time, Dr. Crittenden has been considering the divide that exists between communities of color and longstanding newspaper and television organizations that, in the main, lack diversity in their reporting and editorial staff. He has been exploring ways that the news media's "diversity divide" can be bridged from both ends. "On one end, it is necessary for communities of color to feel engaged in the news gathering and reporting process; and so we are examining the impact of new platforms where news is reported for and by local residents—enabling communities of color to tell news stories in ways that are authentic and representational," Dr. Crittenden explains. On the other end, he is tracking efforts to change newsroom environments, noting, "If newsrooms truly seek to increase diversity within their organizations and improve the range and depth of their coverage, they must find ways to make journalists of color feel they can thrive within their newsroom environments." ■

The Entrepreneurship Gender Gap

Although the number of women-owned enterprises has been growing relatively quickly, only about 40% of new entrepreneurs in the United States are women, notes **Irina Stoyneva, PhD**, assistant professor of management. She studies strategic management and decision making, with an emphasis on how entrepreneurs deal with ambiguity, uncertainty and risk. Recently, she has been considering the factors affecting women's decisions about becoming entrepreneurs.

"Increasing rates of female entrepreneurship could have significant economic benefit," Dr. Stoyneva observes. "To that end, I am studying existing data and applying theories from sociology, feminism and economics to explore what drives the choice of an entrepreneurial career for women." The answers, she is finding, are not straightforward.

In a recent study, she explored this provocative question: "Might reducing the gender gap in career opportunities, economic resources and political engagement serve as a disincentive for women to start businesses?" The research—which drew on country-level data from 89 nations—suggests that while women's equality of economic participation narrows the entrepreneurship gender gap, greater equality within the political and policy spheres widens the gap.

Dr. Stoyneva also found that a country's business regulation efficiency negatively moderates both effects: the positive effect of more women participating in the workforce is weakened and even becomes negative when the efficiency of business regulations is accounted for; but the negative effect of the political participation of women on the proportion of women entrepreneurs is stronger and further reinforced.

"On one hand," Dr. Stoyneva says, "increased gender equality has reduced the resource constraints women often face in launching a business. It also normalizes the societal view of women as 'breadwinners' and perpetuates women's interest in entrepreneurship. On the other hand, family-friendly policies, paid maternity leave and public child care—which all gender-equalize the division of work—negate the need women may feel to start their own business."

These findings suggest just how complex an issue this is—and how rich are the opportunities for studying the most effective ways to address the entrepreneurship gender gap. ■

Irina Stoyneva, PhD
Assistant Professor of Management

Architects of a Sustainable Hemp Industry

For centuries, the hemp plant has been recognized as a robust and renewable source of raw material for a host of purposes. However, for decades United States law conflated hemp with marijuana, and it fell out of use. Now, with such restrictions lifted, hemp has a bright future as a sustainable, high-value raw material for consumer and industrial products.

"Realizing that potential will require a lot of fundamental planning and development work, conceiving and establishing systems and platforms essential for building robust agricultural- and manufacturing-focused hemp industries," says **Ronald Kander, PhD**, associate provost for applied research and dean of Kanbar College of Design, Engineering and Commerce. Success will require the convergence of a broad array of expertise, perspectives and tools—ranging from plant biology, biochemistry and textile engineering, to economics and systems management.

"On the scientific and technical side," Dr. Kander explains, "that work ranges from materials science research on the hemp plant, to the engineering processes that will be used to transform hemp biomass into new materials with unique mechanical, physical or biochemical properties.

"On the business and economic side," he continues, "that work includes characterizing high-value hemp-based products that have well-defined markets; conceptualizing business models and supply chain systems and describing the infrastructure necessary to support a growing industry."

Jefferson is pursuing an array of research and development initiatives that will help make that happen, driven by transdisciplinary teams of faculty and students from engineering, materials science, industrial design, business and other fields. Those teams, in turn, are collaborating with researchers and practitioners from industry and government to conceive an integrated system of new materials, processes, products, business models and regulatory frameworks for a robust and sustainable industry.

"In this context, when we use the word 'sustainable,' we are aiming not just for environmental sustainability," Dr. Kander notes. "We are helping create a hemp industry that is also sustainable economically, technically and in socio-political terms." Toward this definition of a sustainable hemp industry, Kander and his research colleagues are developing a comprehensive Systems Dynamic Model for a complete supply-to-process-to-sale operation. "We intend this model to be an open-source resource that researchers, policymakers, companies and investors can use to simulate results based on their individual data sets and criteria," he explains.

Gurinder Kaur, a PhD candidate in textile science and engineering, is a member of Kander's team. For her doctoral work, she is developing the supply and environmental facets of the comprehensive Systems Dynamic Model. She is using two hemp-derived products now in development as the objects of the model. (See the sidebar, Prototyping Hemp Products.) "As a former manager focusing on sustainable industry supply chains," Kaur explains, "I am enthusiastic because the simulated supply chain model we are developing will create a risk-free method for companies to test the impact of state policy changes—and to do so without fear of losing valuable time and assets."

In addition to guiding the University's overall initiative, Dr. Kander is directly engaged in policy-focused work: he chairs the Pennsylvania Department of Agriculture's Hemp Steering Committee, which is developing a strategic plan for a Pennsylvania-based Industrial Hemp Center of Excellence. And, in parallel with those efforts, Jefferson is helping to develop a vision for the education, training and workforce-development infrastructure necessary to power a growing hemp industry. ■

Prototyping Hemp Products

Over the past few years, a series of industry/University partnerships have led to five "product-by-process" patents for hemp-derived materials—and commercialization is progressing on each of them. Currently, faculty/student teams are working with industrial partners to develop prototypes for two locally sourced and manufactured hemp-based products.

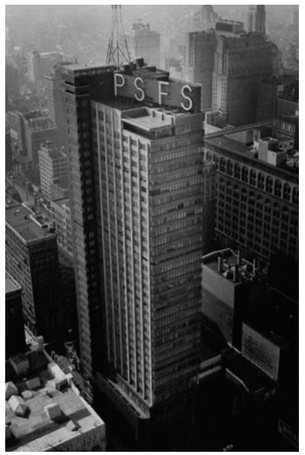
The first uses hemp-reinforced bioplastic for 3D printing. To most effectively capitalize on 3D printing technology for rapid production of customizable and functional products, manufacturers need basic materials with improved physical properties. While reinforced polymer composites could serve that purpose, they are often difficult to recycle and not biodegradable. Jefferson researchers are working with Pennsylvania-based Coexist, Inc. to develop a line of hemp-reinforced polymer 3D printing filaments that are sustainable and biodegradable and have superior physical properties. The project involves processing locally grown hemp and incorporating it into polymers via lab-scale compounding and extrusion processes. By developing this novel material and associated manufacturing process, the R&D team hopes to enable the company to advance new products and processes and be a magnet for new industrial investments.

The second project uses hemp to create injection-molded consumer and industrial parts. Injection molding of polymers and polymer-based composite materials is one of the most common manufacturing processes to make common industrial and consumer products. But these composites can be improved on, both for functionality and environmental sustainability. Therefore, Jefferson researchers are collaborating with Eastern Hemp Company to develop hemp-reinforced polymer-composite injection molding pellets that will allow manufacturers to make sustainable products with superior mechanical and physical properties compared with current polymer-based materials.

Grace Ong Yan, PhD
Assistant Professor of
Interior Design

Architecture, Design and Corporate Modernism

How have business strategies, modern architecture and urban conditions helped shape American corporations' ambitious branding goals? **Grace Ong Yan, PhD**, assistant professor of interior design, addresses that question in her book *Building Brands: Corporations and Modern Architecture*.



Ong Yan is an architectural historian who explores modernism and how media and the built environment intersect. Earlier in her career, she practiced interior design and architecture with Renzo Piano Building Workshop; Pei, Cobb, Freed and Partners and the Gensler New York branding studio. Her book unites her scholarship and design expertise to consider the role of architectural branding in the design of corporate modernism.

"Between the stock market crash of 1929 and the Vietnam War, American corporations were responsible for the construction of thousands of headquarters across the United States," Dr. Ong Yan explains. "Over this time, the design of corporate headquarters evolved from Beaux-Arts façades to bold Modernist expressions. These choices emerged from collaborative efforts by clients, architects and designers to craft buildings that reflected a company's brand while considering consumers' perception and their emotions toward architecture and the messages it communicated."

The book focuses on four American corporate headquarters: the PSFS Building by George Howe and William Lescaze, the Johnson Wax Administration Building by Frank Lloyd Wright, Lever House by Skidmore, Owings & Merrill and the Röhm & Haas Building by Pietro Belluschi. Through them, it shows how design devices of sign, fame, form and material brought company messages to the public. Drawing on original material from corporations' archives, *Building Brands* brings new insights to corporate modernism by examining how company leaders—working with architects—conceived of their headquarters both as workplaces and architectural mediums to communicate company identities and brands. ■

Cold–Brew Chemistry

Despite the growing consumption of cold-brew coffee around the world, little is known about the drink's chemical makeup. Three researchers are helping to fill that gap with new findings on its level of beneficial antioxidants.

A recent study by **Niny Rao, PhD**, associate professor of chemistry, **Megan Fuller, PhD**, former assistant professor of chemistry and pre-medical studies student **Meghan Grim** found that the health-promoting antioxidants in cold-brew coffee can differ significantly from traditional hot-brew coffee prepared with the same beans, particularly for dark roasts. While similar amounts of antioxidants were observed in hot and cold preparations made from lighter-roast coffee beans, the hot-brewing process extracted more antioxidants from dark roasts than the cold-brewing process. Hot-brew coffee from dark-roast beans produce a drink with more antioxidant activity and possibly more health benefits than its cold-brew counterpart.

Pre-medical studies student **Meghan Grim** (right) working with **Niny Rao, PhD**.

> **The health-promoting antioxidants in cold-brew coffee can differ significantly from traditional hot-brew coffee prepared with the same beans, particularly for dark roasts.**

That research built on previous work by Dr. Rao and Dr. Fuller that analyzed chemical differences between hot- and cold-brew coffees brewed with beans of various geographical origins. In that work, they found that the two preparations had similar pH levels. The latest of those studies reported that cold-brew coffee has less acidity (or slightly higher pH values) than the hot-brew counterpart. That is notable because cold-brew coffee has been touted in the media as being less acidic than hot coffee and thus less likely to cause heartburn or gastrointestinal problems.

The researchers are continuing their comparison of the chemical impact of hot and cold brewing processes and of the degree of roast of the beans—focusing next on furans, a group of compounds that contribute to flavor. ■

Do Big Banks Skirt M&A Laws?

Are big banks using insider knowledge of mergers and acquisitions (M&A) to benefit their mutual funds? Banks are not permitted to share private information about their M&A clients' plans with their mutual fund investment managers because advance knowledge of the transaction gives the funds' stock buyers an unfair advantage.

But anecdotal evidence suggests not all banks respect internal information barriers, and **Tim Mooney, PhD**, assistant professor of finance, wanted to see what the hard data said. He reviewed publicly available records on 3,846 mergers, and examined trading activities by mutual funds affiliated with bank M&A advisors.

Dr. Mooney's study—which was the first to focus on particular value-sensitive periods—found evidence consistent with privileged information being shared between investment banking and mutual fund affiliates. "The data demonstrates that bank mutual funds capture high returns by buying or increasing holdings of merger-target companies advised by affiliated investment banks. Moreover, they were more likely to liquidate holdings of target companies planning to withdraw from a proposed merger—before that fact was announced—thus avoiding potential negative returns."

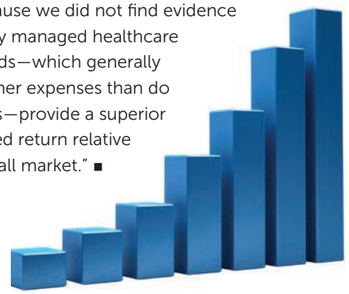
Overall, Dr. Mooney found that bank mutual funds buy stock of about 22% of target companies advised by affiliated investment bankers—but only 2% of takeover-targets where the bank is not involved. "While it's difficult to show causality between a target hiring an investment bank and that bank's mutual funds buying the target's stock, the data suggests that advance knowledge of takeovers flows across bank divisions, from the investment bankers to mutual fund investment managers," Dr. Mooney says. ■

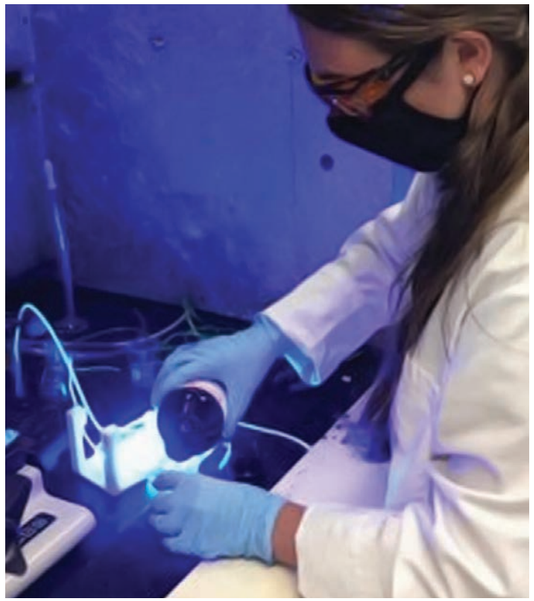
Examining Healthcare Mutual Fund Performance

Specialty mutual funds such as healthcare funds offer investors the opportunity to focus on high total return, income and further diversification within a specific industry. Although extensive research has been conducted on mutual fund performance generally, little such work has been conducted on healthcare-related mutual funds.

D.K. Malhotra, PhD, professor of finance and Nydick Family Term Chair and colleagues, sought to decode the characteristics and performance of healthcare mutual funds by examining their risk-adjusted rate of return from 2001 to 2018. He studied a broad range of healthcare-related funds, including those that focused on pharmaceuticals, biotechnology, health insurance, manufacture of diagnostic supplies and other sectors. The research used multi-prong methodologies to evaluate performance, all of which take risk and return into consideration.

The study found that, on average, equally weighted portfolios of healthcare mutual funds over-performed relative to the Dow Jones Total Market Index and CRSP Value Weighted Index, but underperformed relative to Dow Jones Health Care Index. What are the implications for the average investor? "While investors must make decisions that address their individual goals, resources and risk tolerance," Dr. Malhotra explains, "our study suggests that the average investor in stock funds would be better off including healthcare mutual funds in their overall investment strategy. In addition, it would be prudent to do so through healthcare index funds, because we did not find evidence that actively managed healthcare mutual funds—which generally charge higher expenses than do index funds—provide a superior risk-adjusted return relative to the overall market." ■





Biochemistry student **Brooke Pakech** prepares to conduct a chemical reaction with blue LED light in a 3D-printed flow chemistry device.

Putting Light to Work

Jefferson researchers are using light in new ways: using blue light to drive chemical processes, and creating products that illuminate in ultraviolet light. Their work reflects a convergence of disciplines such as physics, chemistry, textile engineering and nanotechnology that is driving applications with practical benefits for people and the environment.

John Milligan, PhD, assistant professor of chemical and biological sciences, is leading development of environmentally sustainable ways to spur chemical reactions using blue LED light. The work is an example of the "photoredox" subfield of organic chemistry, which has proven to be an increasingly effective method for building organic molecules. In the new approach, blue LED light activates innocuous catalysts to carry out useful reactions. The LED light-driven process could obviate the need for the currently used chemical reagents that produce harmful waste.

In one promising project, Dr. Milligan is working with Jefferson design experts to create 3D printed devices that enable LED light-triggered chemical reactions. Unlike traditional chemistry reactors, light-triggered 3D printed devices could be an inexpensive, easily adaptable and portable method for on-demand preparation of molecules used in medicine or agriculture. The researchers' eventual objective is to synthesize indole alkaloids, which are used in treatments for conditions ranging from cancer to neurological diseases.

"One of the first questions we are trying to answer is whether copper salts can be used with the blue light to make amides, which form the chemical backbone of peptides and proteins," explains Dr. Milligan. "Because copper is abundant, non-toxic and can readily share its electrons with organic molecules to spur reactions, it could be a very environmentally friendly ingredient for synthesizing useful organic molecules."

Another team—including textile engineering and science doctoral candidate **Abdur Sk**, assistant professor of physics **Brian Yust, PhD**, and associate professor of engineering **Brian George, PhD**—is creating ceramic nanoparticles that illuminate under UV light. Then the researchers are incorporating the particles into fabrics and other materials that could be used for a variety of purposes, such as clothing, tools or vehicles.

"To date, nearly all fundamental and applied research on persistent luminescent nanoparticles focused on the visible region of the light spectrum," Dr. George says. "That works well in standard situations—like viewing a watch face in the dark—but not when searching for someone who is lost in a forest or has fallen off a boat."

However, when exposed to UV lights, the new materials can store that energy and then, slowly, emit infrared light that can be easily detected with night vision goggles in low-light situations. The research team's goal is to create materials that exhibit luminescence for a period of hours, which could be life-saving. "Beyond the novelty of incorporating UV-responsive particles in regular products, we believe there will be an array of real-world applications that only begin with search-and-rescue situations," Dr. Yust observes. ■

Computational Intelligence on Eye Disease

"The use of big data in research holds enormous potential for improving public health and healthcare delivery, generating new knowledge more quickly than traditional scientific approaches, and providing a holistic understanding of specific illnesses," says **Amna Al-Alawi, DM**, who recently completed her Doctor of Management degree from Jefferson's Strategic Leadership program. "Ultimately, I believe it can offer enhanced care so that practitioners can understand more accurately the patient's unique combination of genes, environmental risks and disease phenotype, which can help detect certain diseases at an earlier stage."

When Dr. Al-Alawi was contemplating her dissertation, she wanted a topic involving the application of computational intelligence and socio-demographics data to a medical domain. She sought advice from **Les Sztandera, PhD**, professor of computer information systems, whose own work focuses on the application of computational intelligence in business and health care. He arranged for Dr. Al-Alawi to speak with a colleague at LV Prasad Eye Institute (LVPEI) in Hyderabad, India—a longstanding research partner of the Jefferson India Center. That conversation provided the seed for Dr. Al-Alawi's doctoral thesis and for a related journal article—entitled *A Data-Driven Approach for Eye Disease Classification in Relation to Demographic and Weather Factors Using Computational Intelligence Software*—that received the "Best Paper Award" at the Eighth International Data Analytics Conference in Porto, Portugal.

Dr. Al-Alawi used a data-merging technique in her study to combine information from the Telangana (India) State Development Society with the electronic medical record (EMR) of approximately one million LVPEI ocular disease patients. It applied prescriptive and descriptive data analysis techniques to search for insights into high-risk climatic and socio-demographic factors that correlate to the development of cataracts in those patients. Among her findings: a high incidence of cataract in Telangana, especially among women, and the fact that cultural upbringing, climatic factors and proximity to the state-run thermal plant each appear to contribute to the development of cataracts.

Amna Al-Alawi, DM

"The study has proven valuable on at least two levels," Dr. Sztandera suggests. "It has provided a basis for developing new cataract-prevention measures for Telangana residents. And it's hinted at new opportunities for leveraging EMR data to advance ophthalmology diagnostic and treatment methods more generally." ■

Attacking Cancer with Immunotherapies

Jefferson scientists and clinicians continue to advance new approaches for cancer therapies. Two potential immune-prompting treatments—one for solid tumors and advanced non-small-cell lung carcinoma, and a second for recurrent gastrointestinal tumors—entered clinical trials in fall 2020.

The first drug is based on multi-functional immuno-recruitment protein based on a fusion protein platform developed by **Mark Tykocinski, MD**, Jefferson provost and Anthony F. and Gertrude M. DePalma Dean of Sidney Kimmel Medical College. Created through the chimerization of proteins with carefully selected characteristics, the treatment is designed to have a two-part action: first, disabling cancer cells' ability to camouflage themselves from the immune system; then, stimulating proliferation of T-cells that attack the tumor cells. The current Phase I/II multi-center clinical trial is evaluating the drug alone and in combination therapy with an existing PD-L1-blocking checkpoint inhibitor.

"It is exciting to see this novel platform moving forward into clinical development for the benefit of cancer patients," Dr. Tykocinski says. "Its potential as both a stand-alone therapeutic and one used in combination with existing drugs is enormous. The same goes for the pipeline of next-generation immunotherapeutic fusion proteins we are now advancing."

The second drug undergoing trials targets a molecule found throughout the small intestine and colon—guanylyl cyclase C (GUCY2C)—that continues to be expressed when the cells become malignant. The drug acts like a vaccine, inducing the patient's immune system to seek out and kill colon cancer cells expressing GUCY2C. "However, this is not designed to prevent initial development of the cancer," explains **Adam Snook, PhD**, assistant professor of pharmacology and experimental therapeutics. "It is designed to prevent cancer from returning, and is being given after a patient has surgery and other standard therapies, such as chemotherapy." Dr. Snook led the basic and translational research with **Scott Waldman, MD, PhD**, the Samuel M.V. Hamilton Professor of Medicine and chair of pharmacology and experimental therapeutics. **Babar Bashir, MD**, assistant professor of medical oncology, leads the clinical trial operation.

As a vector for prompting the immune system, the vaccine uses a modified version of the common adenovirus that incorporates the spike protein of a rare adenovirus serotype. Having proven the vaccine's safety and efficacy in mouse colon cancer models, the current Phase IIa clinical trial's initial aim is to demonstrate that the drug is capable of safely inducing significant immune responses in colon cancer patients. In addition, because GUCY2C has recently been discovered in gastric, esophageal and pancreatic cancers—which also have high recurrence rates—the trial is enrolling patients with those malignancies. "Our long-term objective is to add this vaccine strategy to the toolkit of therapies for a range of gastrointestinal cancers that together account for about 20 percent of all cancer deaths," Dr. Snook says. ■

"Our long-term objective is to add this vaccine strategy to the toolkit of therapies for a range of gastrointestinal cancers that together account for about 20 percent of all cancer death."

Adam Snook, PhD

Reinvigorating Immune Response to Advanced Melanoma

Melanoma represents a small fraction of skin cancer-related malignancies, yet accounts for the majority of its mortalities—and the incidence of cutaneous melanoma is rising. While treatments using small-targeted inhibitors and immune checkpoint antibodies have increased long-term survival in advanced-stage cutaneous melanoma, many patients still do not realize any benefit from the treatments. Another group of patients initially have beneficial results but ultimately find their disease progressing, in part due to cancer cells' acquired resistance to immune response. And still other patients have difficulty with the treatment's high toxicity.

Emad Alnemri, PhD, Thomas Eakins Professor of Biochemistry and Molecular Biology, and **Andrew Aplin, PhD**, Kalbach-Newton Professor of Cancer Research, have been leading a series of studies of the molecular processes that determine whether or not current inhibitor and immune checkpoint treatments will work well in melanoma patients, and for how long. Now, based on the results of those studies, they are working to develop new, more-effective treatment approaches that address three goals: triggering a robust anti-tumor immune response that has significant clinical effect, preventing onset of acquired resistance and minimizing patient toxicities.

Over the past two years, their research team announced a series of important findings that help to address the question of why initially successful immune system-focused therapies for patients with stage III and stage IV melanoma often fail within 13 months, due primarily to tumor cells acquiring resistance to the drugs. "Previously, the field has lacked detailed knowledge of exactly how targeted inhibitors and immune checkpoint agents work together to fight melanoma tumors—how they prompt both tumor-cell death and alterations in the tumor-immune environment," Dr. Alnemri explains. "However, our studies have described a molecular mechanism of targeted inhibitor regulation of an immune-stimulatory form of cell death. In identifying the mechanism, we have been able to describe a proof-of-principle therapy concept for melanoma tumors that are resistant to inhibitor-based treatments."

A key to the new therapeutic approach is the researchers' discoveries on the molecular mechanisms by which the gasdermin E gene and its expressed protein function. The gasdermin E protein normally participates in the cell-death program—which, among other purposes, is intended to kill malignant cells. And in many cancers, gasdermin E expression is much lower than it is in healthy cells.

The researchers found that gasdermin E participates in the cell-death process by spurring creation of holes in a cell's outer membrane and its mitochondrial membrane. "Next," Dr. Aplin says, "looking at the role that gasdermin E plays in malignancies, we found that cancer-cell lines without gasdermin E multiplied about twice as fast as normal cells. Moreover, in mice models of melanoma, cells lacking gasdermin E grew larger tumors—where, in contrast, cancer cells retaining some gasdermin E expression had slower growth."

Thus, Drs. Alnemri and Aplin concluded, gasdermin E could provide several clinical opportunities. "Not only could it be used as a marker to distinguish aggressive tumors from less-aggressive ones," Dr. Alnemri explains, "it could be employed to help design effective treatment strategies."

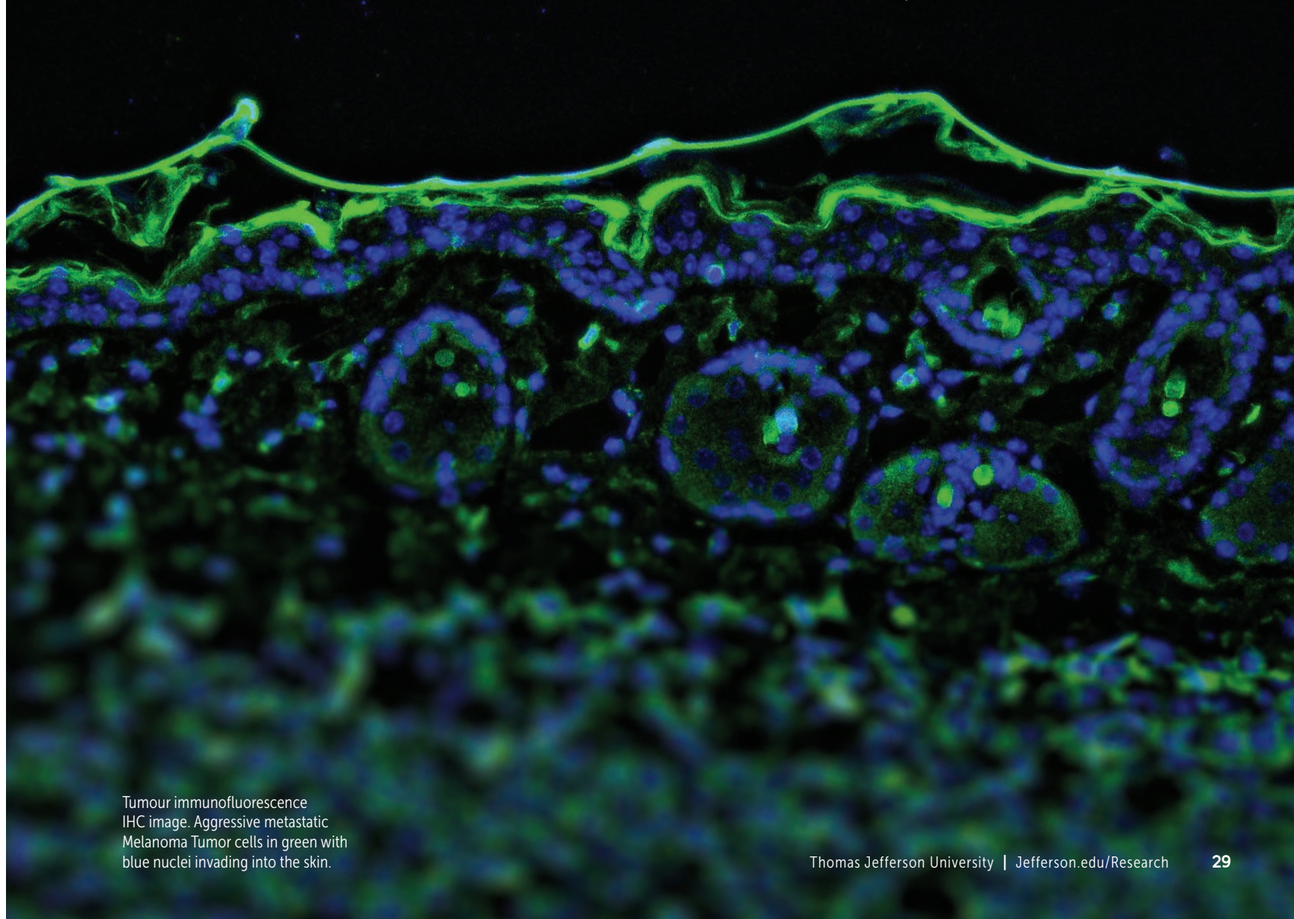
Perhaps more exciting is the potential for using gasdermin E as a new therapeutic target.

To that end, they are now developing approaches for promoting gasdermin E expression as a method for reinvigorating the immune system in melanoma tumors that have proven resistant to current treatments. "In simplified terms, we are working to boost and restore the immune system's natural ability to kill melanoma cells," says Dr. Aplin. "And we hope that it may also prove effective in other cancers where gasdermin E expression is suppressed." ■

New Target for Treating Triple-Negative Breast Cancer

Triple-negative breast cancer is an aggressive and difficult to cure form of the disease—and is prevalent in Black and Latinx women. With his research colleagues, **Adam Bailis, PhD**, associate dean for research in the Jefferson College of Health Professions, has been exploring the potential of a protein named RAD52 to be an effective target for drugs that fight the condition. RAD52 is a factor in the tumor suppression network that, when mutated, can reduce the risk of breast cancer in carriers of the BRCA2 gene mutations that are associated with many breast cancers. In the first report of the protective effect of RAD52, the researchers identified two potential mechanisms for suppressing tumorigenesis in BRCA2-deficient cells. And their continuing work provides further evidence that the RAD52 gene may be a promising target for drugs that kill BRCA2-related cancers.

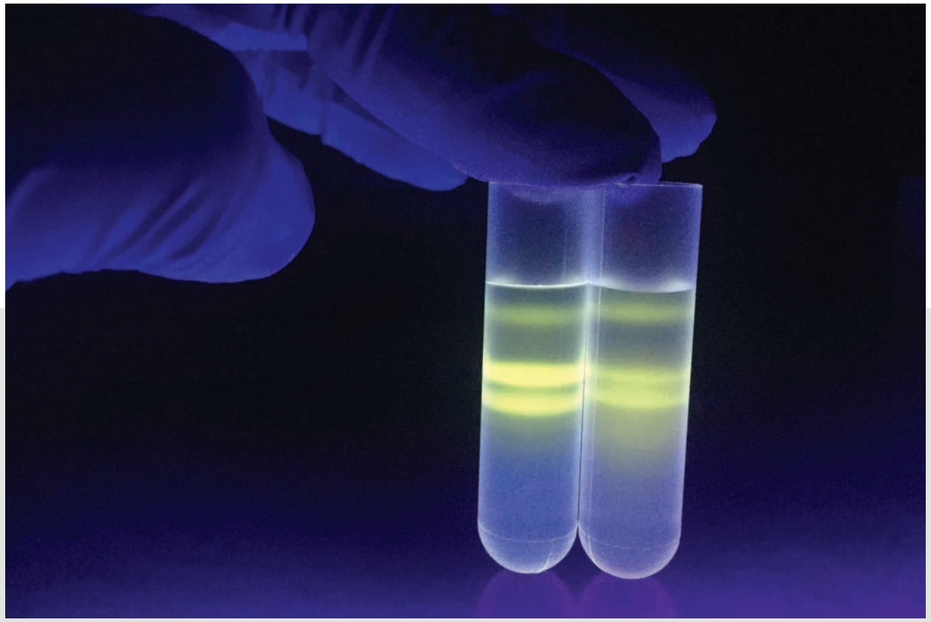
This body of work complements major efforts by Sidney Kimmel Cancer Center at Jefferson investigators to understand DNA repair regulation in cancer, and to tailor cancer therapies for DNA repair-defective tumors.



Tumour immunofluorescence IHC image. Aggressive metastatic Melanoma Tumor cells in green with blue nuclei invading into the skin.

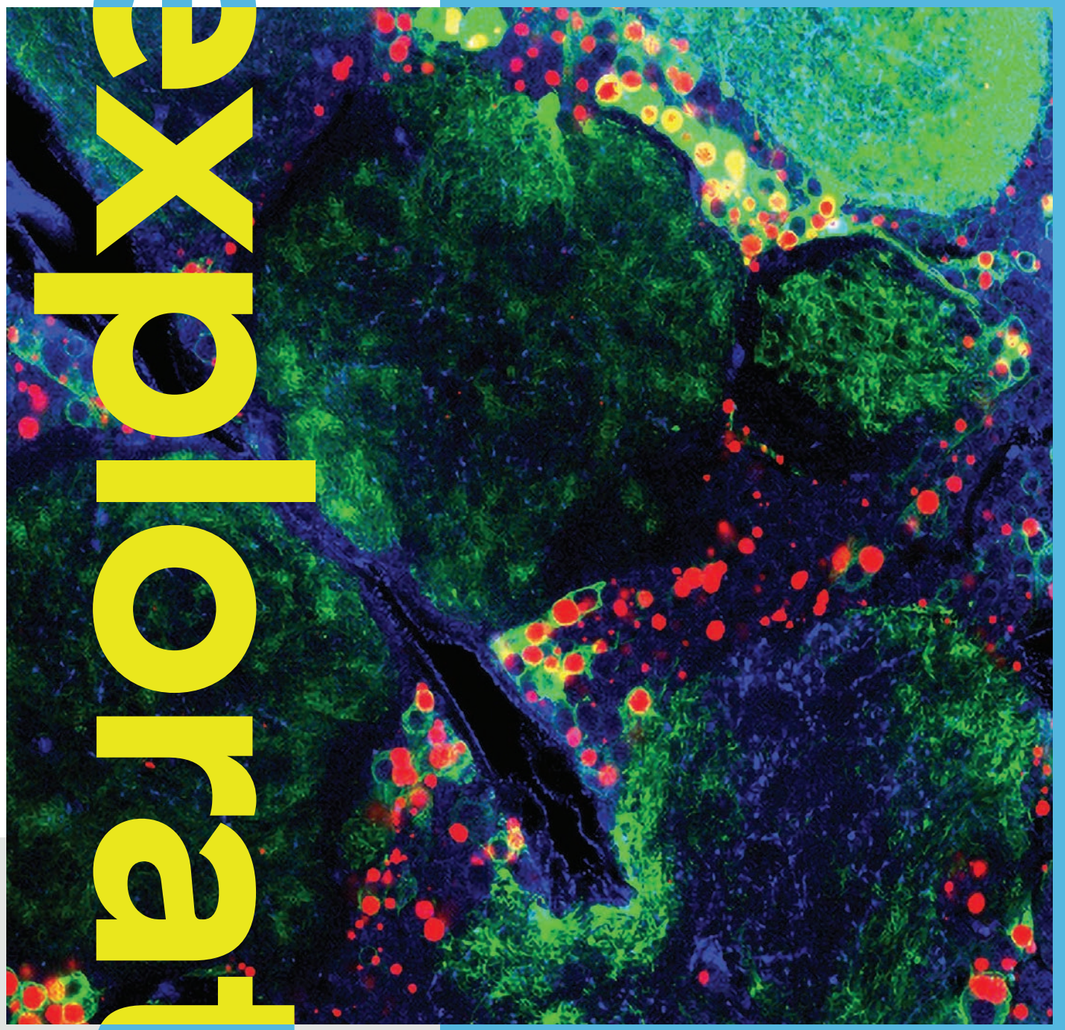
Images of Exploration and Discovery

There are many ways of capturing the phenomenon and processes that biomedical researchers investigate. Steady advances in imaging technologies provide windows into microscopic forms and functions—views that can be appreciated, in different ways, by scientists and nonscientists alike. Here are a small sample of the images that emerge from the work of Jefferson researchers. ■

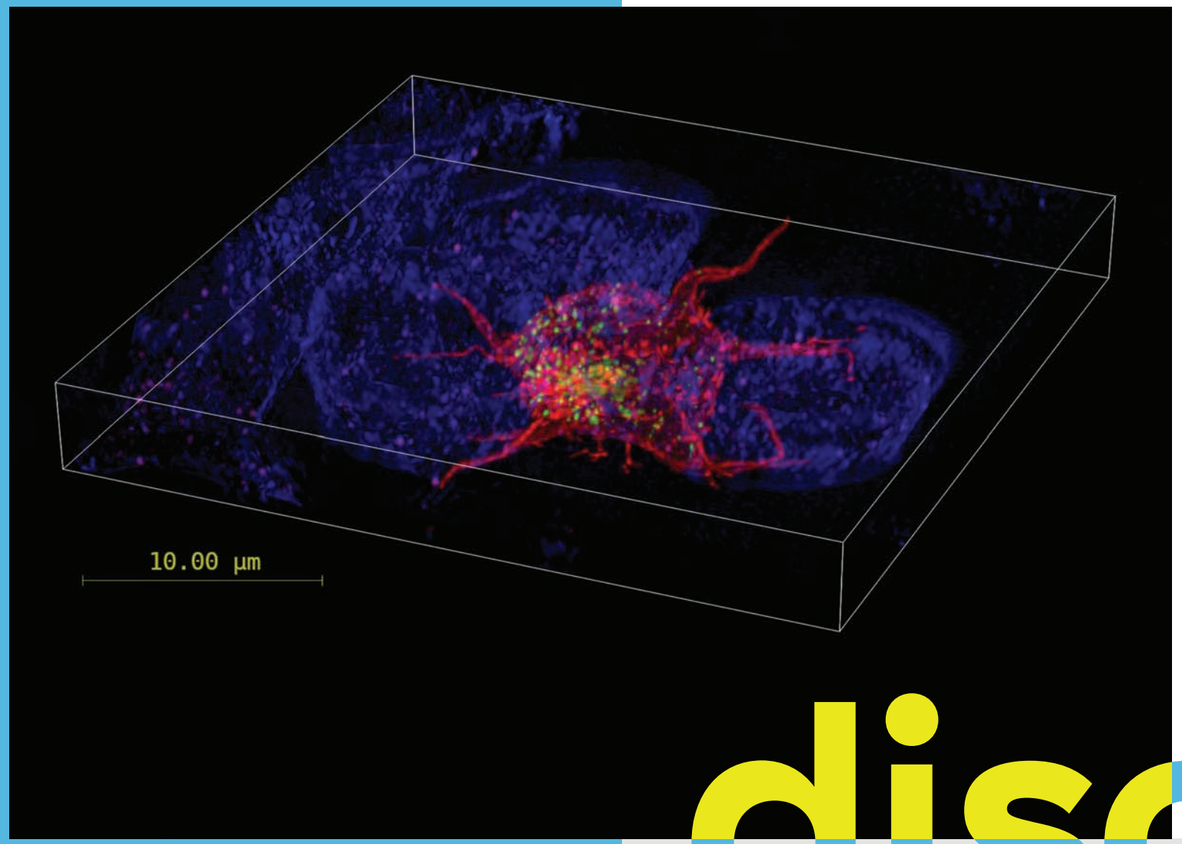


↑ Postdoctoral and graduate student researchers in the lab of **Dmitry Temiakov, PhD**, associate professor of biochemistry and molecular biology, are investigating how transcription and replication of mitochondrial DNA is regulated in different types of human cells. This unmagnified image shows highly purified human mitochondrial DNA—which the researchers isolated using density gradient centrifugation—glowing under the UV light.

exploration



↑ The lab of **Tim Mosca, PhD**, assistant professor of neuroscience, studies fruit fly olfaction as a means to understand how connections in the brain form and function. To tell the difference between different smells in the environment, the brain uses specific neurons—called interneurons—to compare environmental signals. As seen in this confocal microscopy image of the fruit fly brain, interneurons (red) express particular chemicals (blue) to communicate with the rest of the brain (green).

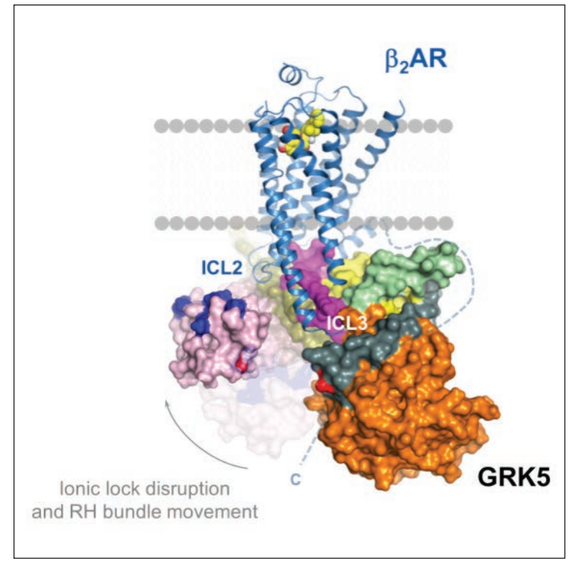


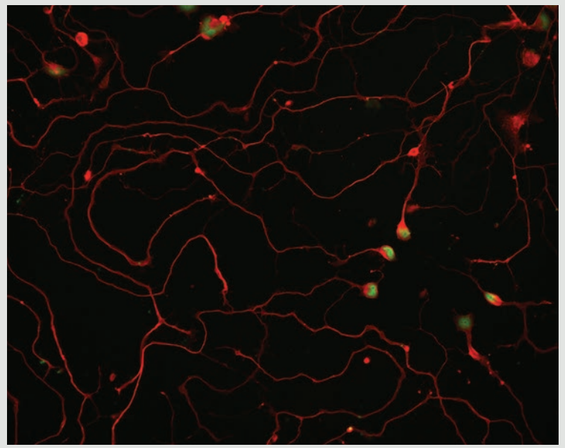
discovery

↑ Researchers in the lab of **Claudio Giraudo, PhD**, associate professor of microbiology and immunology, used super-resolution stimulated emission depletion (STED) microscopy to create this 3D projection of an engineered human CD8 Lymphocyte (in red) releasing the content of cytotoxic granules (green) during the destruction of tumor cells (blue).

→

Jeffrey Benovic, PhD, Thomas Eakins Endowed Professor of Biochemistry and Molecular Biology, and his research colleagues are renowned for discoveries on the function, signaling and regulation of G Protein-Coupled Receptors (GPCR), which are important in processes that ultimately control cell growth, cell motility and other functions. This molecular model—developed through mass spectrometry analysis and hydrogen deuterium exchange-mass spectrometry studies—is enabling scientists to suggest new strategies to regulate GPCR signaling in human disease.





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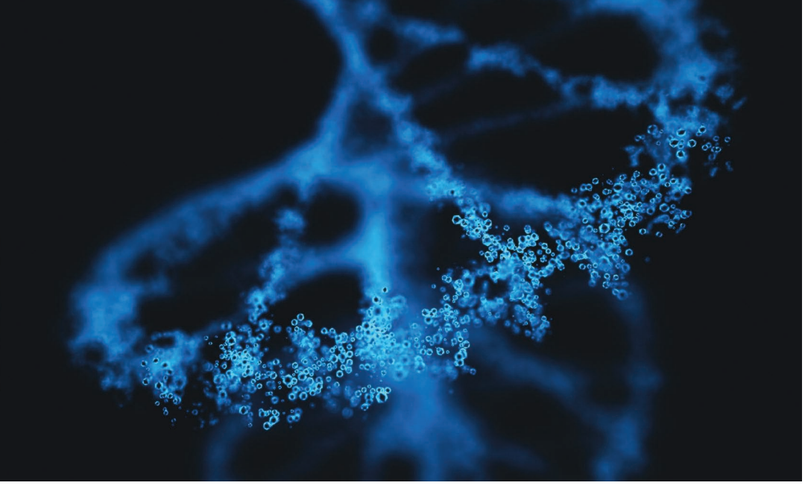
This automated fluorescence microscopy image—created by a neuroscience doctoral student in the lab of **Diane Merry, PhD**, professor and vice chair of biochemistry and molecular biology—captures the state of induced pluripotent stem cells (red) as they differentiate into mature motor neurons (green). This work is part of the lab's evaluation of the mechanisms underlying motor neuron degeneration in spinal and bulbar muscular atrophy.



Exploring DNA Damage Repair

A cell's ability to repair damaged DNA is key to its maintaining normal biology and protecting against cell death. But the repair process can be a two-sided coin: keeping a normal cell healthy is beneficial; keeping a malignant cell healthy can promote cancer. The mechanisms by which cells recognize and attempt to repair damage are myriad and complex; and individual DNA-repair proteins can be involved in multiple pathways. Jefferson researchers across several fields are working to understand the genomic and molecular processes at work in DNA repair—and the problems created when those processes go awry.

Anna Pluciennik, PhD, research assistant professor of biochemistry and molecular biology, studies DNA repair processes in the central nervous system and their connection to neurodegenerative disorders. In particular, she is working to understand genomic and molecular mechanisms underlying conditions such as Huntington's disease and spinal and bulbar muscular atrophy that are caused by a large number of repeated nucleotide sequences in neurons' DNA. The extensive repeats lead to aggregation of proteins in the nucleus that cause cell death. Dr. Pluciennik is studying a series of genes involved in the DNA repair process that have been implicated in Huntington's disease — working to tease apart the effect of each of these "mismatch repair" genes on the development of the extensively repeated sequences. She is also using patient-derived induced pluripotent stem cells in an effort to identify ways to intervene in the processes that create the protein aggregations. Dr. Pluciennik observes that, "An array of neurodegenerative diseases preferentially afflict older individuals. Given our aging population, it is important to better understand age-related changes in DNA repair capability—as well as the impact of long-term accumulation of DNA damage."

Elise Fouquerel, PhD, assistant professor of biochemistry and molecular biology, is exploring the roles played by proteins called Poly (ADP-ribose) polymerases (PARPs) in chromosomal stability and the development of malignancies. Dr. Fouquerel—who has received a prestigious NIH "Pathway to Independence Award"—is studying how PARPs contribute to the maintenance of telomeres under stress conditions. Telomeres are DNA segments that protect the ends of chromosomes from progressive degradation and from unnecessary attention by repair systems that mistake the chromosome ends for breaks in its strands. But telomeres themselves can be broken down, leaving chromosomes vulnerable to damage that turns the cell malignant. Dr. Fouquerel's research has demonstrated how chronic oxidative stress accelerates telomere shortening; and she is now exploring PARPs' role in protecting telomeres from that stress. "Given the critical role of telomere crisis in driving carcinogenesis, this work could have important implications for development of therapies that address the ways that oxidative stress drives tumor development," she explains.

Matt Schiewer, PhD, assistant professor of urology and cancer biology, is also studying the roles that PARPs play in development of malignancies. His objective in focusing on these DNA repair-enzymes is to spur development of new ways of treating prostate and bladder cancer. In one current study, he is defining the downstream biological consequences of PARP function and examining the respective roles of two PARP pathways. "Ideally, we will identify points in these pathways that could be targeted to interrupt prostate tumor development," Dr. Schiewer says. He is also conducting a series of studies that, he hopes, "will revolutionize our understanding of PARP function in bladder cancer, delineate the consequences of PARP activity in this tumor type and clarify the best way to implement PARP inhibition-based treatments. ■

Studying HIV Antiretroviral Therapy

Combination antiretroviral therapy (ART) has turned HIV infection into a treatable, chronic condition, rather than one that is almost inevitably fatal. As a result, as they age, people with HIV often begin taking other medications to treat medical conditions ranging from heart disease to gastrointestinal problems to cancer. The increased number of medications creates a risk for drug-drug interactions. **Jason Schafer, PharmD**, professor and vice chair of pharmacy practice, is exploring combinations of ART drugs that can reduce the number and severity of those interactions.

> **Researchers found that significant reductions in the incidence and severity of drug-drug interactions occurred when patients' ART regimens were changed to include a category of drugs known as integrase inhibitors.**

One major study he led was a multicenter, retrospective study that analyzed patients on ART who were also taking medications for cardiovascular disease, neurologic and psychiatric disorders, chronic pain, inflammation, gastrointestinal/urologic conditions or conditions requiring hormonal therapy. Previously, 57 percent of the patients studied had experienced at least one interaction. However, the researchers—who included current pharmacy doctoral candidate **Ciara Walshe** and then-students **Nick Hastain, PharmD** and **Aleena Santana, PharmD**—found that significant reductions in the incidence and severity of drug-drug interactions occurred when patients' ART regimens were changed to include a category of drugs known as integrase inhibitors.

In related research, Dr. Schafer—working with then-students **Kaitlin Sassa, PharmD** and **Jackie O'Connor, PharmD**—found that some patients experienced unintentional weight gain when switching their ART medications. Exploring the effect further, the investigators evaluated those weight changes as well as changes in cholesterol, glycemic control and cardiovascular disease risk following specific ART switches. The results of the study suggested that patients may experience weight gain, increased cholesterol and increased Atherosclerotic Cardiovascular Disease Risk Scores. Dr. Schafer has since initiated a follow-up study evaluating long-term changes in weight and cholesterol following ART changes with doctor of pharmacy students **Matty Zimmerman**, **Ciara Walshe** and **Jessie Cerankowski**. ■

Participants of a recent Institute-sponsored project developed a vision for a public transit hub at Sheba Medical Center.

Toward Smarter, Healthier Cities

"Creating healthy cities is perhaps the great challenge of this century, and the move to smart cities gives us the opportunity to make health a part of every neighborhood, every block," observes **Stephen K. Klasko, MD, MBA**, president of Thomas Jefferson University and CEO of Jefferson Health. "We can now diagnose what's wrong in urban life and find solutions in real time."

The Institute for Smart and Healthy Cities was launched in 2020 to support multidisciplinary research, innovation and education on the transformation of urban environments into more efficient, healthier and livable cities. A collaborative initiative of the College of Architecture & the Built Environment, the College of Population Health and Kanbar College of Design, Engineering and Commerce, the Institute is catalyzing learning, exploration and technology development partnerships across the University—and with businesses, nonprofit organizations and public agencies. It represents Jefferson's intention to drive convergence of the myriad fields of knowledge necessary for effectively addressing the complex challenges that cities face in coming decades.

Institute director **Edgar Stach, Dipl.-Ing.**, professor of architecture, notes that, "We start from the perspective of cities as complex, inter-related systems; and we are helping faculty and students address the most pressing and connected challenges—housing and workplaces, public health, environment, energy and transportation in urban regions." Reflecting that transdisciplinary approach, the Institute's associate directors are **Russell K. McIntire, PhD**, assistant professor of public health, and **Tod Corlett, PhD**, William L. Jasper Chair and professor of industrial design.

The Institute pursues research programs that address three scales. Urban scale projects will, for example, analyze population behavior changes through data-driven analysis, modeling, and simulation and visualization, and will use statistical modeling to

Continued »

Some student designs for the "City of Health" project at Sheba Medical Center.

predict changes in health, energy and transportation. Building scale projects will predict the effects of daylighting and natural ventilation on health outcomes in work, life and healing spaces, and can help develop and predict health benefits of new concepts for net-zero energy buildings. Finally, device scale projects will develop people-centric building controls and management technology, and will allow us to study the interconnectivity between data on human health and measures of micro climate and air pollution.

In one of the unique interdisciplinary research and design projects done under the Institute's oversight, a team of architecture, industrial design and occupational therapy students and faculty worked with counterparts at three Israeli institutions—Bezalel Academy of Arts and Design, Shenkar College of Engineering, Design and Art and globally respected Sheba Medical Center—to develop concepts for Sheba's "City of Health" initiative. The project showcased how forward-looking industrial and architectural design can creatively and productively help shape the emerging healthcare landscape.

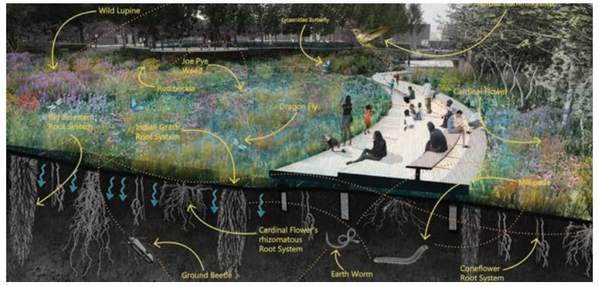
The project's specific objectives included developing a three-phase master plan for the Sheba campus's physical future. The plan included methods for bolstering public transportation—including new transport hubs and light rail stops—as well as pedestrian-friendly environments and biking paths. It also identified opportunities and potential products for aging-in-place, including devices that enable older patients to better find their way around campus, and public seating specifically designed to help them sit down and then stand up easily.

"Our group sought to address a series of real-life challenges experienced by the Medical Center's patients, caregivers, visitors, and surrounding community," Dr. Stach explains. "The result was a series of creative solutions at many levels—from major buildings to individual patients' concerns." ■

Beauty in the Commonplace

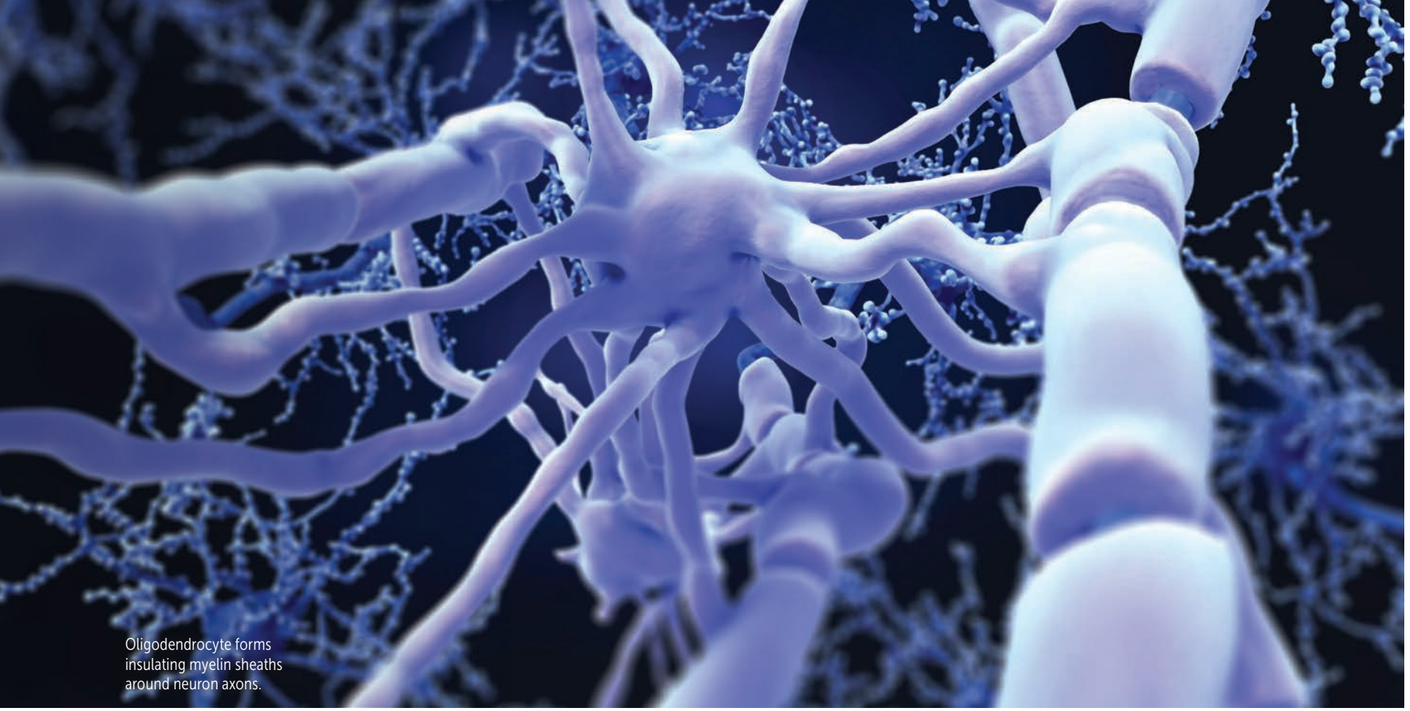
In 2020, undergraduate landscape architecture student **Benjamin Nardi** received a top award from the American Society of Landscape Architecture for his plan to turn a one-acre urban brownfield site into a space filled with native flora and fauna and urban agriculture. His dual goal: responding to the hopes, dreams and concerns of the area's residents; and connecting them to the land's watershed roots. "I wanted to give voice to people traditionally without much of a voice. This is their design, not mine," says Nardi. ■

One of Nardi's first steps: imaging the existing site through sketches and photographs.



Nardi's plan included a detailed approach for reestablishing native wetland flora.

The "Bird's Nest" feature, enabling residents to be in closer touch with urban fauna.



Oligodendrocyte forms insulating myelin sheaths around neuron axons.

Paradigm-Changing Immunotherapy for Multiple Sclerosis

In multiple sclerosis (MS), the body's immune system attacks the myelin sheath, the protective layer surrounding nerve axons. Current MS therapies act by suppressing the immune system broadly—with sometimes serious side effects, including infection and cancer. However, a team of researchers led by **Abdolmohamad Rostami, MD, PhD**, professor and chair of neurology, has found a way to prevent immune cells from attacking myelin—while leaving the rest of the immune system intact. In mouse models of MS, their approach has halted disease progression.

"One of the biggest hurdles to stopping the attack on the myelin sheath is that science doesn't know which component of myelin is triggering the immune response in MS patients," says Dr. Rostami. "Previous studies have tested the use of single myelin antigens or combinations of antigens to prevent autoimmunity, but those methods have had limited clinical success."

Dr. Rostami's team took a different approach: using oligodendrocytes, the type of cell that produces the myelin sheath that wraps around axons. Oligodendrocytes contain tiny sacs called extracellular vesicles (EVs) that—the researchers found—contain almost all the relevant myelin antigens. The team harvested EVs from cultured oligodendrocytes to create a therapy with the potential to treat the disease without having to know the exact identity of the effective antigen.

> **"While the antigens involved in the autoimmune response can differ between MS patients—and even change over time in an individual patient—the fact that our approach was effective in different experimental models shows this could act as a universal therapy."**
>
> Abdolmohamad Rostami, MD, PhD

"We then injected the EVs intravenously in mice that modeled different stages of MS," Dr. Rostami explains. "When administered before the disease developed, the EVs had a prophylactic effect, preventing the onset of symptoms like decreased mobility and paralysis. When given after disease onset, EVs significantly reduced severity of symptoms." Of particular note, the experimental therapy only affected immune cells that were attacking the myelin layer. The rest of the immune system was intact and not weakened at all.

"While the antigens involved in the autoimmune response can differ between MS patients—and even change over time in an individual patient—the fact that our approach was effective in different experimental models shows this could act as a universal therapy," observes Dr. Rostami. "This is one of several major advantages over current therapies."

Working on a parallel research path, Dr. Rostami's team has also found that a compound of naturally occurring elements may both reduce and help reverse MS's damage to the myelin sheaths covering axons. "Although the evidence is preliminary, our studies suggest that ursolic acid—a compound found in the peels of fruits such as apples and prunes, and some herbs—can both halt and repair damage in animal models of disease," says **Guang-Xian Zhang, PhD**, professor of neurology. The researchers used a lab-grade purified form of ursolic acid in a mouse model of MS that develops slowly, mimicking human disease; and they began the treatment at an advanced stage, when chronic tissue damage had already affected the nervous system.

"After 20 days' treatment, we began to see improvement in the animals' function; and after 60 days' treatment, those that were initially paralyzed had regained the ability to walk, although with weakness," Dr. Zhang explains.

Analyzing the mechanism for the improvement, the investigators observed that ursolic acid has two important effects: It suppressed Th17 cells—immune cells that help drive the pathological autoimmune response in MS—and spurred maturation of oligodendrocytes, thus enhancing the myelin sheath-making process. "This maturation effect on oligodendrocytes is crucial," says Dr. Zhang. "In MS, myelin sheath-making oligodendrocytes are depleted, and the stem cells that produce new oligodendrocytes are unable to mature. This compound helps activate those stem cells and is likely responsible for the reversal of symptoms we observed."

Although ursolic acid is available as a dietary supplement, it could be toxic at high doses. "A number of tests are necessary to ascertain that this compound is safe before initial clinical trials begin," says Dr. Rostami. "However, we are moving forward quickly with this promising approach." ■

How Does Calcium Impact Cardiac Mitochondria?

The ability of a cardiac cell to work hard and continuously depends on the energy-producing function of its mitochondria. Calcium is key to proper mitochondrial function—but only in the right amounts. Too much calcium leads to cell death; too little suppresses production of the fuel a cell needs to function.

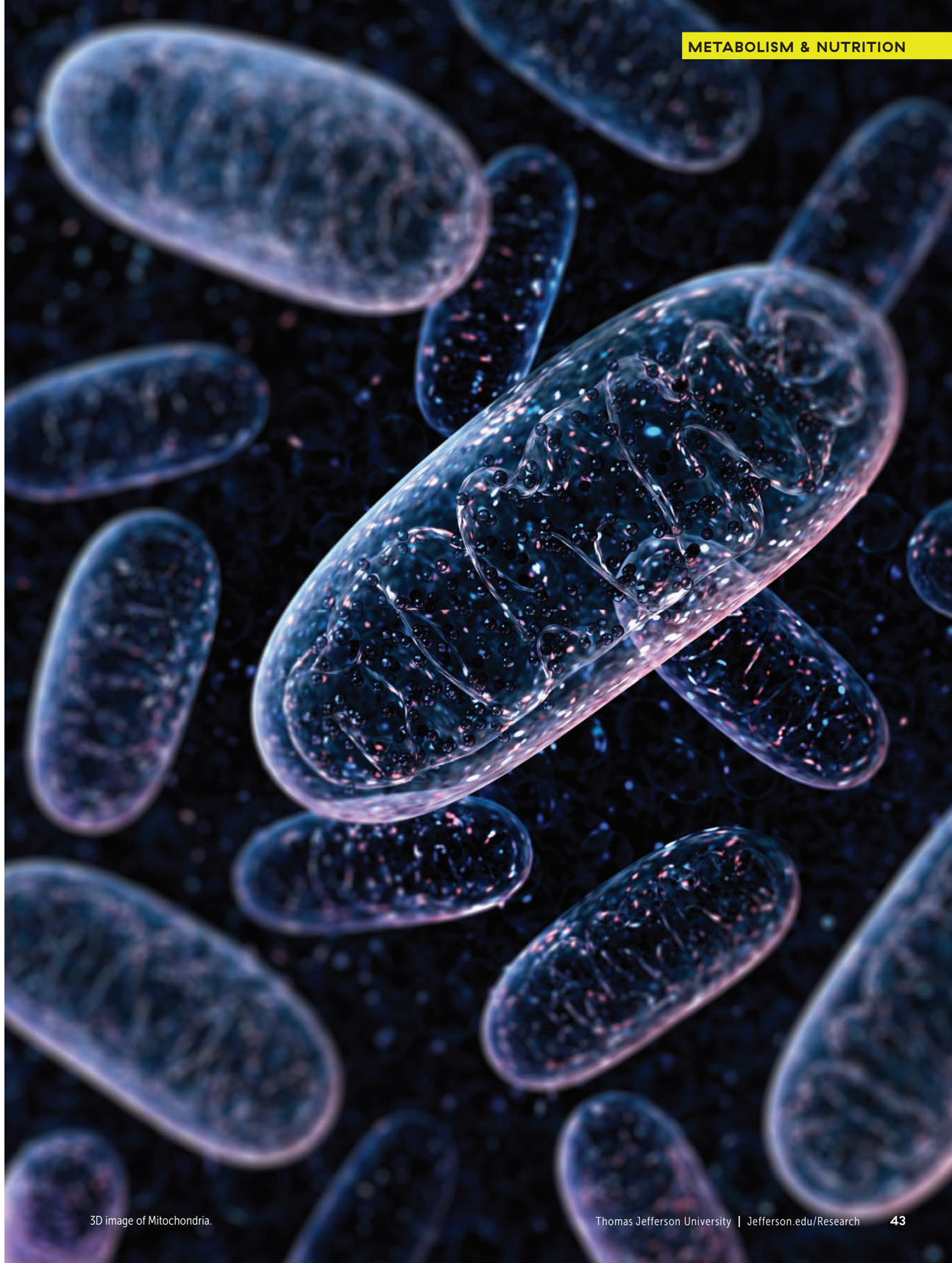
Research collaborators **Shey-Shing Sheu, PhD**, professor of medicine, and **Gyorgy Csordas, MD**, research associate professor of pathology, anatomy and cell biology, are studying the mechanisms by which cardiac mitochondria use calcium and other molecules. And they are shedding light on how dysfunction in those mechanisms contribute to ischemic heart disease, cardiac arrhythmias and heart failure. Currently, Drs. Sheu and Csordas are engaged in three related NIH-funded studies.

The first study is probing the function of the mitochondria's inner membrane, which regulates the transport of ions and metabolites including calcium. The opening of an inner-membrane structure called the permeability transition pore (PTP) can cause mitochondrial swelling that, if sustained, leads to cell death. The researchers are working to determine, among other mechanistic questions, how increased calcium concentration opens the PTP. "In addition," Dr. Sheu says, "the study is exploring whether different forms of the PTP could provide a relief valve for excess calcium. That would offer a potential target for drugs that prevent cardiac cell damage."

The second study explores the role that excessive activation of a specific protein—called dynamin-related protein 1—plays in persistent PTP opening. "This work will help us better understand how a healthy heart can perform perpetually in the face of enormous workload and what goes wrong to lead to heart failure," explains Dr. Sheu.

Finally, the third study seeks to better understand how the calcium released from a cellular structure called the sarcoplasmic reticulum of dyadic junction—which initiates muscle contraction—enters the mitochondria. As Dr. Csordas explains, the researchers believe that the new knowledge gained in this study will help explain how this process contributes to regulating the energy metabolism of the heart—and factors into the dysregulation that leads to cardiac disease. ■

> **"The study is exploring whether different forms of the PTP could provide a relief valve for excess calcium. That would offer a potential target for drugs that prevent cardiac cell damage."**
>
> Shey-Shing Sheu, PhD



3D image of Mitochondria.

Invasive Plants for Commercial Use

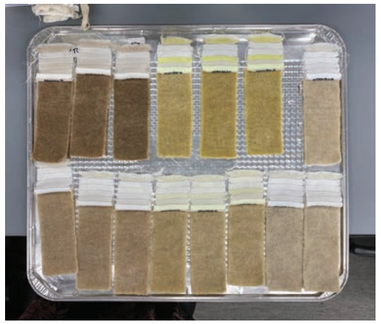
Wineberries—macro closeup showing detail and texture.

Invasive plants can have an array of negative ecological effects. In Northeast deciduous forests, for example, invasive plants outcompete natives, disrupt soil nutrient cycling and spread disease that affects humans as well as other plants.

"Invasives are creating increasingly difficult problems across the United States," says **Anne Bower, PhD**, professor of biology. "While there are some public and nonprofit efforts to address those problems, we also need to employ free market incentives to overcome this major ecological challenge." Dr. Bower, **Mary Ann Wagner-Graham, PhD**, assistant professor of biology, and **Becky Flax, MS**, assistant professor of textile design, have been working with an interdisciplinary group of undergraduate researchers to develop and demonstrate one such approach: using invasive plants to create natural, non-toxic, sustainable alternatives to synthetic dyes.

The researchers' first step was selecting the plants to use in their experiments. "We sought invasives that have potentially useful properties for creating textiles and which are known to create problems for human health or ecological balance," Flax explains. They chose three specific types of plants to investigate: Japanese barberry, which supports black-legged tick populations and, thus, promotes higher incidences of Lyme disease; wineberry, which hosts viruses affecting native herbaceous species; and Oriental bittersweet, which causes trunk failure in native species.

Biology student **Irene Cooper** cuts fabric samples to be treated with invasive plant-based dyes.



Fabric colors created with invasive dyes include coffee, latte, dusty, rose and citro.

In the initial phase of a multifaceted project, the researchers—who included students from the pre-medical sciences, biology, health sciences and textile design programs—harvested roots of those types of plants in the Philadelphia area. Then they processed the roots to create an array of dyes that were used to treat hundreds of pieces of organic cotton or wool fabric. "The students then assessed the resulting color quality and color durability," Flax says. "In addition, they analyzed the dyed fabrics' antimicrobial properties, compared to control fabrics. While neither wineberry nor bittersweet showed significant microbial inhibition, barberry demonstrated antimicrobial action against Escherichia coli and Staphylococcus aureus—which could make it useful in dying outdoor furniture and work apparel."

What's next in this multi-phase project? Having analyzed dyes from the roots of the three invasives, the researchers will conduct detailed experiments on the dying and antimicrobial capacities of the plants' berries, stems and leaves. But they won't stop there, Dr. Bower notes: "This research initiative is not focused solely on harvesting and using invasive plants. We will complete the environmental restoration process by replanting the grounds with resilient species native to the region." ■

Immune Signals in Parkinson's Disease

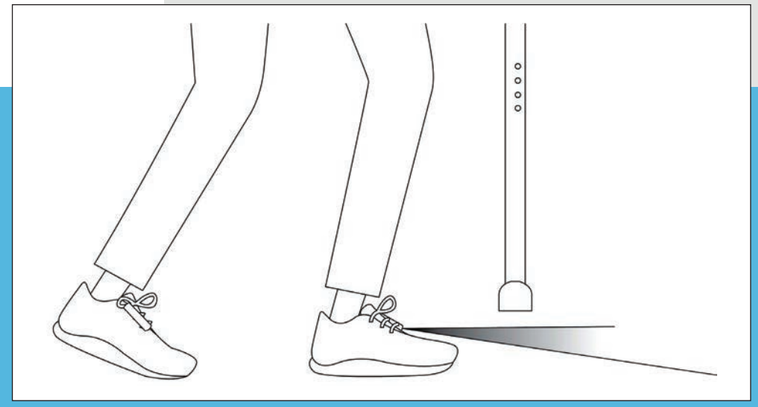
The Jefferson Comprehensive Parkinson's Disease Center is one of the Parkinson's Foundation's 33 Centers of Excellence in the United States. Its director, **Richard Smeyne, PhD**, professor of neuroscience, and his research group are examining the cell signaling and cascade of events that leads to initiation of Parkinson's disease (PD), seeking important clues about ways to arrest the condition's progression. Mutation within the Leucine-rich Repeat Kinase 2 (LRRK2) gene is thought to underlie about 20 percent of all PD cases. Two of the group's recent studies suggest that immune signaling from T-cells and B-cells in the blood plays an unexpected and important role in development of LRRK2-related PD.

The first of these studies explores neuro-inflammation—one of the most common pathologies seen in PD—where specialized brain cells release chemicals that lead to neuron death. To understand how this process starts and is regulated, researchers led by senior postdoctoral fellow **Elena Kozina, PhD**, looked at the way that LRRK2 gene mutations affect inflammation in mice. When they administered a compound that mimics bacterial infections, they found that only mice with LRRK2 mutations showed PD-like effects in the brain. These effects included an exacerbated brain inflammation that appeared to arise from signals initiated in T- and B-cells in the blood. This finding has the potential to provide new targets for interfering with the onset and progression of PD; it could also lead to identification of blood-based biomarkers that could be used as an "early warning" of PD.

In the second study, the researchers explored the impact of substituting a normal mouse immune system for one that has LRRK2 mutations. Would it "rescue" the mice from PD-like pathologies? They pursued this question in a creative way: generating a new strain of mice that contained LRRK2 mutations in all cells, but lacked an immune system; then using bone marrow transplantation to give the mice a normal immune system. Thus, the mice had normal LRRK2 in their T- and B-cells, but LRRK2 mutations in other cells, including all their brain cells. These chimeric mice could then be used to directly test the notion that signals from the peripheral immune system (the T- and B-cells) prompted inflammation in the brain—and that not having LRRK2-mutated immune cells would prevent PD-like symptoms.

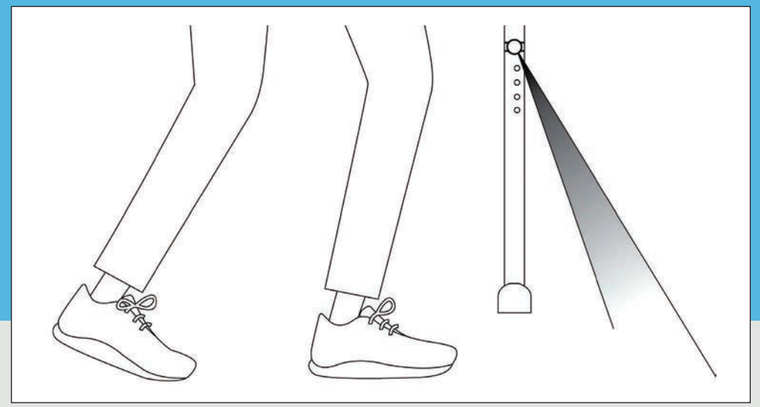
> **This finding has the potential to provide new targets for interfering with the onset and progression of PD; it could also lead to identification of blood-based biomarkers that could be used as an "early warning" of PD.**

"Our hypothesis proved correct," Dr. Smeyne says. "Much of the mice's brain-immune response was normal; no neuron death was observed. This important finding points to a new way to think about how PD starts, and we are examining if this 'crosstalk' between the peripheral immune system and the brain is at work in other forms of PD." ■



One of the unique aspects of Thomas Jefferson University is that students from the Kanbar College of Design, Engineering and Commerce have the opportunity to interact and work with neurologist **Tsao-Wei Liang, MD**, to develop novel and practical devices to help patients with PD.

Through a summer work-study program, design students have been invited to the Movement Disorders clinic to evaluate the daily struggles of patients, return to the studio and then brainstorm to create and develop prototypes that have the potential to improve the quality of life of persons with Parkinson's.



Applying New Knowledge for Parkinson's Patients

Beyond its leading program of basic and translational research into the biological mechanisms underlying Parkinson's disease, the Jefferson Comprehensive Parkinson's Disease Center leverages the University's broad range of capacities in clinical and applied research. For example, the Center's active clinical research and experimental therapeutics program runs clinical trials that range from evaluating novel delivery systems for levodopa and testing adjunct medications for motor complications to assessing new systems for deep brain stimulation therapy and gauging the impact of nutritional support for PD patients.

On the applied end of the research spectrum, Jefferson design students work with **Tsao-Wei Liang, MD**, associate professor of neurology, to develop novel and practical devices to help patients. The students observe and learn about the daily struggles of patients in the Center's Movement Disorders clinic; then they return to the design studio to conceive and develop prototypes of products with real potential to improve quality of life of those patients.

Brain Implant Aims to Restore Movement After Stroke

In the United States, someone has a stroke every 40 seconds. Often, these victims have long-term physical disabilities—the inability to use an arm and hand properly, for example. While rehabilitation can restore some function, improvements typically plateau well short of full recovery. Seeking to help stroke patients gain a fuller return-to-function, a research group led by assistant professor of neurology **Mijail Serruya, MD, PhD**, has begun a clinical trial of a brain implant and motorized robotic brace that could enable greater mobility. The work represents a convergence of disciplines, including computer science, fashion design, mechanical engineering, neurology, physics and rehabilitation medicine.

In this trial, a recovering stroke patient has had electrodes implanted in the brain. The electrodes are connected to a mechanical brace intended to help replicate normal movement and restore physical abilities. "The electrodes send signals originating in brain neurons to an arm brace that then controls movement," explains Dr. Serruya. Bioengineer and visiting professor **Alessandro Napoli, PhD**, led development of the computer software that translated the patient's brain signals into control commands for the arm brace.

Most previous research on such "brain-computer interface" (BCI) systems has focused on individuals with extensive disability, such paraplegia resulting from spinal cord injury. However, the Jefferson study is striving to help the majority of stroke victims, who have significant but less extensive disability. "The current trial serves as a proof of concept that our electrodes can effectively convey neuronal signals to a mechanical device that guides and supports arm movements for stroke patients," Dr. Serruya says. "We view this trial as a bridge to implanting wireless electrodes that can convey those signals to an effective device."

Perhaps most notable, "This study is the first to implant electrodes in a patient who can walk and still live semi-independently," says Dr. Serruya. "What we're studying is much more relevant to all of the people who live with disability from stroke. But for that reason, it's also more challenging." While the brains of most patients who previously participated in BCI studies are relatively healthy (because their injuries occur in the spine or lower brain), Jefferson researchers have implanted electrodes adjacent to the stroke-damaged area. "As a result, we must regularly adjust and refine the artificial intelligence algorithms that interpret brain signals in order to have movement that best reflects a patient's intention. But we believe this work will inform all future BCI trials for fully implantable and wireless devices," notes Dr. Serruya.

Dr. Serruya works closely with the patient to adjust the brain-computer interface.

> **"We believe this work will inform all future BCI trials for fully implantable and wireless devices."**
>
> Mijail Serruya, MD, PhD

Neurosurgeon **Robert Rosenwasser, MD, MBA**, led the electrode-implantation surgery for the patient in the current Jefferson trial, accompanied by neurosurgery colleagues **Ash Sharan, MD** and **Chengyuan Wu, MD**. "We have long seen stroke patients go home and struggle with simple daily tasks like picking up a cup of coffee or brushing their teeth. But this approach, which helps restore function, could in coming years be a game changer for our patients," says Dr. Rosenwasser, chair of neurological surgery and president of the Vickie and Jack Farber Institute for Neuroscience at Jefferson Health. "Fully implantable BCI electrodes are being developed by a number of companies, and this trial will pave the way for a future in which a patient with permanent disability from stroke can get an implant, train with rehab and artificial intelligence experts to use it, and go home with finer control of a mechanized brace."

The clinical trial's success depended on the diverse types of knowledge and skills of an interdisciplinary team that—beyond Drs. Rosenwasser, Napoli and Serruya—included an occupational therapist, physical therapist, neuroradiologist, stroke specialist neurologist, multiple biophysicists, and associate professor of fashion design **Anne Hand**, who created a customized coat for the patient to wear when using the mechanical brace outdoors in cold weather. Several Jefferson medical and occupational therapy students were also involved in the effort. ■

Assessing Trauma's Effects on Children

"Children who are exposed to adverse experiences early in life may not think, feel or behave the same way that typically developing children do," says **Kirby L. Wycoff, PsyD**, associate professor of counseling and behavioral health and director of Jefferson's Community and Trauma Counseling program. "If behavioral health professionals are not cognizant of the effects of trauma in the lives of children, they may actually be providing ineffective and inefficient care—and doing a disservice to the children and their families."

> **"Complex trauma can alter brain structure and function and throw children off a normal developmental trajectory, resulting in myriad negative outcomes."**
>
> Kirby L. Wycoff, PsyD

Dr. Wycoff is co-author of *Essentials of Trauma-Informed Assessment and Intervention in School and Community Settings*, a book that offers step-by-step guidelines for health professionals conducting trauma-informed assessments and interventions. Drawing on Dr. Wycoff's extensive experience working with children, adolescents and families in community and school settings, the book provides detailed coverage of how early experiences of trauma and toxic stress can put children at risk for academic, social-emotional, behavioral, neuropsychological and mental health problems. And it presents expert guidance on incorporating a trauma-informed, resiliency-focused perspective into practice for assessment, consultation and evidence-based interventions.

"Complex trauma can alter brain structure and function and throw children off a normal developmental trajectory, resulting in myriad negative outcomes," Dr. Wycoff explains. "We wrote the book to promote a deeper understanding of the use of assessment data to inform interventions in practice. It's designed to help busy practitioners and school psychologists quickly acquire the knowledge and skills they need to make optimal use of major psychological assessment instruments." ■

Canine Intervention for PTSD

Strong anecdotal evidence suggests that trained service dogs can help mitigate symptoms of post-traumatic stress disorder (PTSD) and traumatic brain injury (TBI). In particular, they may help reduce incidence of substance abuse and suicide in military veterans with PTSD and TBI. Two Jefferson College of Nursing faculty members—assistant professor **Jennifer Shiroff, PhD**, and instructor **Jacquelyn O'Rourke-Fulford, MSN**—have begun the process of formally assessing the effectiveness of service dogs as a therapeutic intervention for veterans with PTSD or TBI.

"Service dog use has increased over two decades, but there is a lack of definitive information about impacts and little standardization of implementation," says O'Rourke-Fulford. Therefore, Dr. Shiroff explains, "We are beginning to build a foundation of scientific evidence to support clinical guidelines for determining medical necessity, as well as standardization of prescriptive practices and training of service dogs."

Dr. Shiroff and O'Rourke-Fulford are collaborating on the initial stages of the research with Leashes of Valor (LOV), a nonprofit that helps connect veterans with service dogs that are specifically trained to recognize and help manage PTSD and TBI symptoms. Indeed, Jefferson College of Nursing's canine "chief compassion officer" Maggie—a LOV-trained Labrador—helps improve mental health in the University community through companionship and affection.

In parallel work, **Erin Eller**—a student completing a master's degree in pharmacology—is developing the protocol for a clinical trial intended to provide evidence on effectiveness and impact of trained service dog intervention. The trial could provide data that would help demonstrate whether the intervention is worthy of insurance reimbursement, which would be key to expanding availability of service dogs to veterans in need. ■

Chief Compassion Officer Maggie, accompanied by military veterans **Jason Haag** and **Danique Masingill**, two of the founders of Leashes of Valor.

Measuring Empathy Among the Healthcare Team

We live in a time when empathy seems more important than ever. Two recent studies assess opportunities and challenges for training physicians and nurses to develop stronger skills in empathy.

Jefferson research professor of psychiatry and human behavior **Mohammadreza Hojat, PhD**, led a nationwide study of empathy in nearly 11,000 osteopathic medical students in the United States. The study used the Jefferson Scale of Empathy (JSE), a validated measurement tool developed at Jefferson and used in 85 countries and translated into 56 languages. Among its findings were that women tended to score higher on the empathy scale than men, and students of African American and Hispanic/Latinx descent tended to score higher than those of white or Asian descent. In addition, it found that students planning to pursue specialties such as internal medicine, family medicine, pediatrics and psychiatry tended to score higher than those focusing on specialties such as anesthesiology, pathology, radiology and surgery.

In previous research, Dr. Hojat has demonstrated that empathy has a significant role in improving patient care—finding, for example, that physicians who scored relatively high on the JSE rendered better care to their diabetic patients. Now, he observes, "the recent study's specific findings can be used to identify those who may need more help than others to enhance and sustain their empathic orientation toward patient care. And, more broadly, it confirms that empathy in patient care can be measured by a psychometrically sound instrument, and can be evaluated to support professional development of physicians-in-training and in-practice. Measures of empathy could also be employed in making admissions decisions for medical school and residency training programs, and to guide career counseling and specialty selection."

Looking at one specific facet of empathy within nursing education, research from assistant professor of nursing **Karen Alexander, PhD**, indicates that existing training approaches may not adequately challenge nursing students' pre-existing assumptions about poverty. Indeed, the findings suggest, counterintuitively, that previous experience of poverty may reduce students' empathy by reinforcing societal stigmas.

"We should train nurses to empathize with patients in poverty and to help eliminate healthcare disparities," says Dr. Alexander. "Toward that end, our research asked whether past experiences with poverty—either directly experienced or observed through volunteer service—gave nurses a stronger sense of empathy towards populations experiencing poverty."

For the project, she and her colleagues used the JSE and collected data on students' exposure to poverty, plus their age, gender, ethnicity and religion. They were surprised to find that personal experience with poverty often did not correlate with higher empathy scores. More surprising: students who had interacted with poverty through volunteer experiences—such as working at soup kitchens—had lower empathy scores than their cohorts. Dr. Alexander notes, "The volunteer experience is central to a lot of medical and nursing-school learning, based on the idea that such exposure is sufficient to counter students' ingrained assumptions and beliefs about people in poverty. But it may not have that effect. In fact, our results suggest that service learning isn't enough and may actually be detrimental—with students bringing their biases into volunteer experiences and having those biases confirmed, not challenged." Dr. Alexander and colleagues are pursuing further research to test that hypothesis and to assess other factors that may be at work. ■

Collaborating to Address Complex Needs

In the United States, patients with complex health and social needs drive a disproportionate share of healthcare costs: approximately five percent of patients—those with high needs and high use—account for about half of the nation's healthcare expenditures. Moreover, despite their frequent inpatient and emergency room usage, the care these patients receive often fails to address their individual mix of medical, social and behavioral needs.

Jefferson's Student Hotspotting curriculum, offered by the Jefferson Center for Interprofessional Practice and Education (JCIPE), enables teams of students from eight professional healthcare disciplines to learn about the challenges faced by patients with complex health and social needs—and to work collaboratively to help patients navigate the challenge of getting effective health care. Recently, faculty began to formally assess whether students who participate in the program demonstrate increased knowledge of, comfort with and empathy toward medically and socially complex patients. The study's preliminary results indicate that Hotspotting student participants exhibit greater self-efficacy and empathy than a control group of nonparticipating students—and that the gap between the two groups widens over time.

While the study continues, it appears that this kind of collaborative, interprofessional, hands-on education program has great potential to enhance health professionals' ability to provide patient-centered, team-based care to people with complex health and social needs—and, in the process, reduce healthcare expenditures and improve lives.

Does Art Reduce Bias Among Healthcare Providers?

Katherine Cambareri, who earned an MPH from Jefferson in 2019, works as a clinical research coordinator at Children's Hospital of Philadelphia. She is also a serious photographer and deeply interested in exploring the synergies between public health and art.

In 2016, Cambareri created a photographic exhibition by documenting the clothes worn by survivors of sexual violence when they were assaulted. The exhibit's photographs—individually straightforward, collectively powerful—were created with the intention of increasing understanding of sexual assault and challenging false assumptions of those who blame the victim. The exhibition titled "Well, What Were You Wearing?" has been presented across the country and featured by numerous media outlets, including *Huffington Post*, *Self* and *Time*.

"I wanted people to think about victim blaming and to recognize that asking, 'What were you wearing?' is not a valid question," Cambareri says. "Beyond the fact that a person's choice of clothing does not justify assault, sexual violence does not only happen to people who dress a certain way, in a certain style or wear a certain size. The stereotype that victims are always wearing revealing clothing when they are assaulted is false."

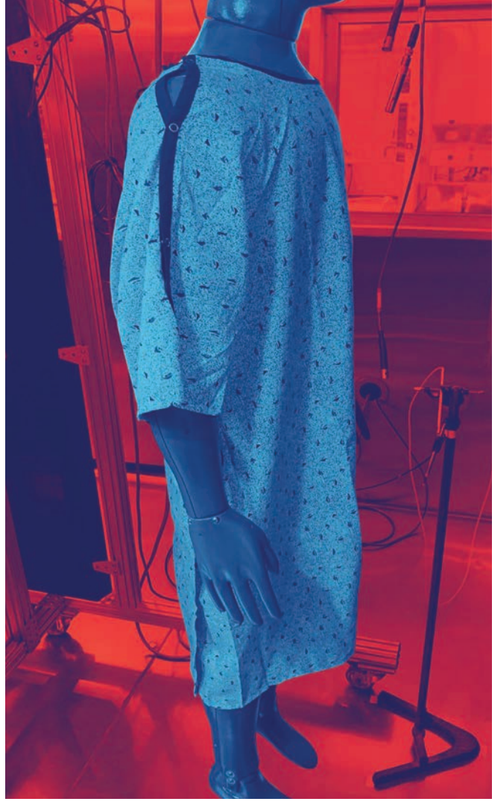
Today, she and **Rosie Frasso, PhD**, professor of population health, are collaborating with MPH students **Jules LaRosa**, **Amanda Guth** and **Veronique Hooper** on a multifaceted study exploring the exhibit's potential impact on the perceptions that future healthcare providers have of survivors of sexual violence. Results from a pilot study, which indicate a positive response to the approach, were presented at the American Public Health Association meeting in October 2020. The team will expand the project and engage medical, nursing and physician assistant students from several Philadelphia area institutions.

"We know that a traditional lecture can help future healthcare providers better understand bias and stigma regarding sexual assault," Dr. Frasso says. "But we want to understand if exposure to the exhibit's visual content can have a fuller, lasting impact—if a visit to this exhibit is 'stickier' and could help reduce bias when those providers engage with victims years from now."

Cambareri says, "It has been extremely rewarding knowing that the exhibit has been able to give a voice to sexual assault survivors. Now, it is exciting to see my public health work and art collide to increase the opportunity for that voice to be heard by future nurses and doctors." ■

"I wanted people to think about victim blaming and to recognize that asking, 'What were you wearing?' is not a valid question."

Katherine Cambareri



Testing the thermal resistance of a patient gown using a thermal sweating manikin in Bruner Materials Characterization Laboratory.

A Design for Mitigating Patient Hypothermia

General anesthesia during surgery can impair the body's autonomic temperature regulation and lead to patients having dangerously low body temperature. That, in turn, increases an array of clinical risks, including poor wound healing and infection, excess blood loss, cardiac arrhythmias and impaired renal function. Unfortunately, current surgical gowns—which have very little thermal capability—provide no significant protection against heat loss.

For that reason, a cross-disciplinary team of Jefferson students and faculty—with expertise in anesthesiology, mechanical engineering, textile engineering, textile technology and fashion design—is creating a new type of patient garment that is intended to mitigate the problem of surgically related hypothermia.

"Our goal is to design a cost-efficient patient gown that provides thermal insulation before, during and after surgery," explains **Ryan Masoodi, PhD**, associate professor of mechanical engineering, who leads the development team with anesthesiologist **Adam Thaler, DO**. Dr. Thaler notes, "In a typical surgery, when patients go from the operating room to post-anesthesia care, we usually use approximately 10 blankets to keep each one warm. Our group thinks there must be an approach that is both more effective and efficient." For example, one approach the team is considering: a multi-layered reusable gown that binds a layer of infrared material—intended to reflect heat back onto the patient's body—between a fabric inner layer and a woven polyester outer layer.

"As a multifaceted team backed by technical resources such as the Bruner Materials Characterization Laboratory and the Textiles Engineering program, we have the capability to solve a problem that is universal across hospitals," says mechanical engineering undergraduate **Lexi Patania**. Her fellow mechanical engineering major **Jenna Yorko** adds, "If we are successful, this product has the potential to be put into use in operating rooms throughout the world."

Having completed preliminary research on the clinical challenges and on the limitations of current approaches to combatting hypothermia, the team developed a design-planning process that is the basis for a grant application now being reviewed by the National Institutes of Health. ■

JeffSolves with Student Innovation

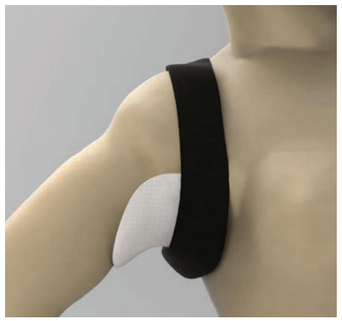
The JeffSolves MedTech program teams industrial design and medical students to develop innovative solutions to specific healthcare problems. Having chosen particular, concrete challenges faced by medical patients, student teams collaborate to conduct in-depth user research and problem identification, develop potentially marketable solutions and create prototype products. "The solutions these teams create are consistently remarkable and effective," says **Bon Ku, MD**, assistant dean for health and design at Sidney Kimmel Medical College.

In 2020, JeffSolves teams created three innovative, important products. *Callicore* is a car seat for pediatric patients immobilized in hip spica casts following surgery for hip dysplasia or femur fractures. *Conexo* is the first product providing barrier protection for IV connection sites, thereby preventing bacteria from entering the bloodstream. *Steam 'n Spin* is a low-cost, easy-to-use breast pump sanitizer designed for NICU-grade pathogen control and high-volume use.

JeffSolves' immersive accelerator experience—just four years old—is already seeing its solutions move toward the marketplace. ALAFLEX is a JeffSolves 2017 spinout launched to market an ergonomically designed, three-dimensional, axillary bandaging system for individuals with *hidradenitis suppurativa* (HS), in which excessive leakage and extreme pain cause significant medical problems and impair quality of life.

ALAFLEX co-founders in the Health Design Laboratory (from left): Abhishek Umashankar, Victor Hsue, Haru Jang and Leena Ramani.

"Although millions of people suffer with HS, there was no ideal dressing, but now the patent application for our product is pending," explains ALAFLEX co-founder **Victor Hsue**, a 2020 graduate of Sidney Kimmel Medical College, who is now an otolaryngology resident. His co-founders are fellow graduates **Leena Ramani** and **Abhishek Umashankar**—now pursuing residencies in, respectively, internal medicine and emergency medicine —and **Haru Jang**, a 2018 MSID graduate, now an Industrial Designer and UX Researcher at DiveDesign. ■



The ALAFLEX bandaging system.

Can Textiles Improve Emotional Wellbeing?

"As a textile designer, I am very interested in challenging perceptions of what a textile can be," says **Kristen Tynan**, whose master's thesis, "Seeking Solace," explored the creation of textiles that provide specific tactile benefits.

It's known that tactile stimuli help calm negative emotional sensations. Thus, children may seek a favorite blanket or toy, and adults may use more reflexive, inconspicuous strategies like light foot-tapping or employ stress balls and fidget spinners. But those tools are primarily stand-alone objects marketed toward children or people with neurological challenges such as autism spectrum disorders.

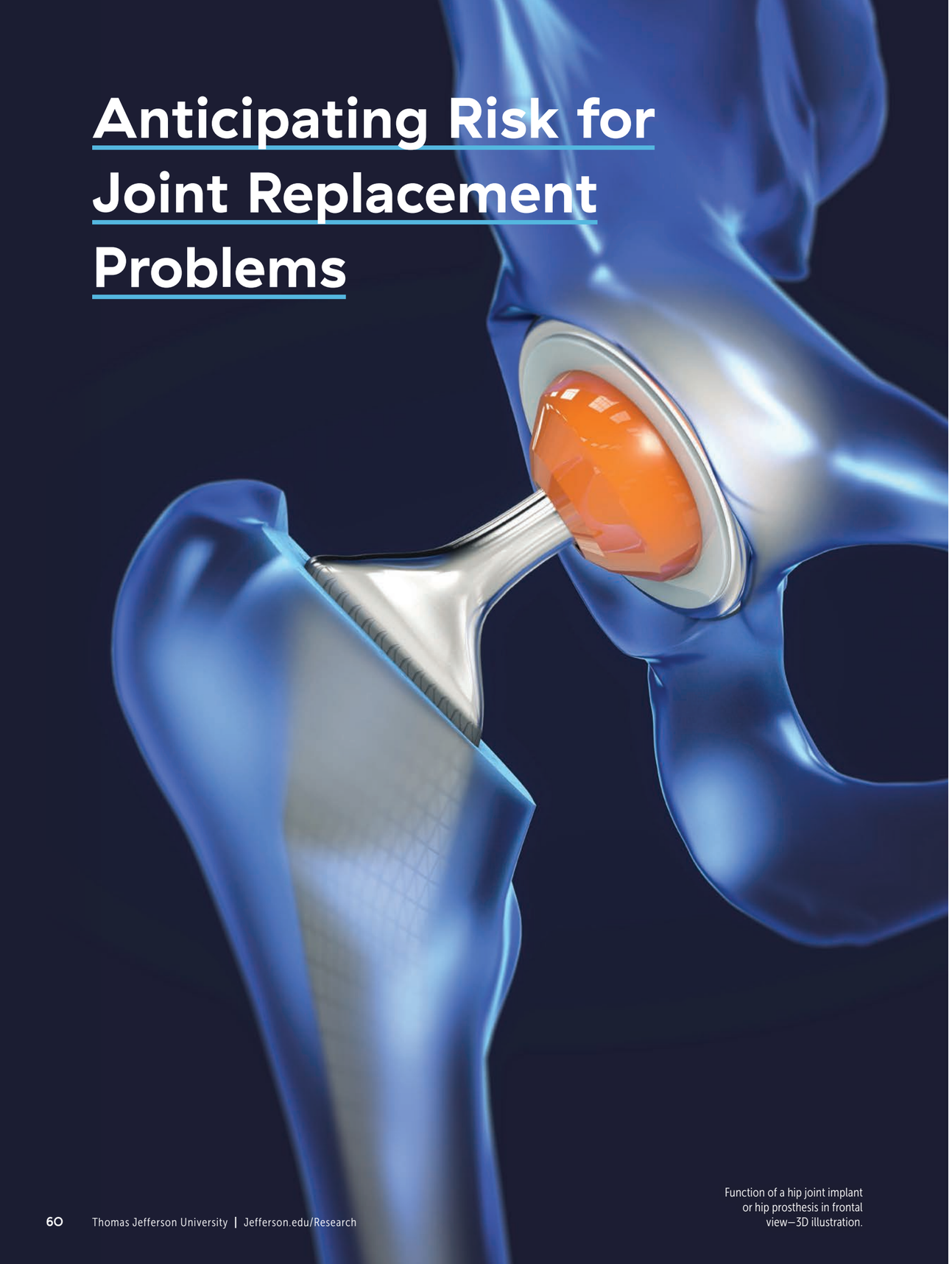
> **"I believe that as a main component of our interior spaces, textiles could be the vehicle with which to incorporate meaningful sensory input into our environments."**
>
> Kristen Tynan

"Now, imagine if this kind of sensorial input was a design criteria for our interior spaces. What would that look like? More importantly, what would that feel like?" Tynan asks. "I believe that as a main component of our interior spaces, textiles could be the vehicle with which to incorporate meaningful sensory input into our environments."

Thus, her project investigated the role textiles could play in enhancing emotional wellbeing by seamlessly integrating purposeful tactile-sensory input into spaces where we live, work, sleep, dwell, commute and wait. Toward that end, she created and evaluated a collection of fabrics with specific tactile qualities. "This collection is really just the beginning of my exploration of what it would mean for sensory fabric to be readily available in any space—not just auxiliary or 'therapeutic' spaces," she says, "and of how such fabrics could provide distinct emotional and physiological benefits addressing an individual's needs at any given moment." ■

Student **Kristen Tynan** is shown "in the field" conducting research about tactile benefits of textiles.

Anticipating Risk for Joint Replacement Problems



Function of a hip joint implant or hip prosthesis in frontal view—3D illustration.

Research teams led by **Javad Parvizi, MD**, clinical research professor and vice chair of orthopedic surgery, have identified risk factors associated with two major postoperative issues for patients undergoing total hip or knee replacements.

Despite ongoing improvements in technology and perioperative protocols, some patients undergoing total joint arthroplasty (TJA) experience serious medical complications requiring postoperative intensive care. With TJA increasingly being performed in ambulatory surgical settings, it is important to understand which patients are most at risk for such complications. Dr. Parvizi and his colleagues conducted a study to identify patient risk factors for admission to an intensive care unit (ICU) following elective total hip (THA) and total knee (TKA) arthroplasty. The researchers used data on 12,342 THA patients and 10,976 TKA patients—132 and 114 of whom, respectively, had an unplanned postoperative ICU admission.

For both sets of patients, the study found multiple independently associated factors for increased risk of ICU admission. Those factors included (but were not limited to) older age, bilateral procedure, revision surgery, increased Charlson comorbidity index, increased estimated blood loss, increased preoperative glucose and decreased preoperative hemoglobin. Increased body mass index was an additional factor for knee procedure patients. All the procedures included in the analysis were done at a high-volume center with surgeons specializing in joint reconstruction. "Thus the findings may not be generalizable to all facilities and practices," Dr. Parvizi explains. "However, we do believe that, in general, identifying risk factors for admission to the ICU following elective TJA may help surgeons risk stratify patients and allow for higher-risk surgeries to be performed in facilities where an ICU is available."

Periprosthetic joint infection (PJI) is one of the most pressing clinical issues in orthopedic surgery, resulting in additional surgeries, longer hospital stays and poor outcomes for patients. Dr. Parvizi led a group of researchers in examining the use of irrigation and debridement (I&D) surgery, which is usually reserved for patients presenting with acute PJI. While the procedure is helpful for some patients, data suggests that failure rates for the intervention range between 30 and 80 percent. "Having an objective assessment tool to predict if a PJI patient is likely to benefit from I&D surgery would help in treatment decision-making," says Dr. Parvizi.

His group conducted the study using data previously collected for an international, multicenter study of 1,174 revision THA and TKA arthroplasty patients—34.4 percent of whom had failed treatment with I&D. The study found 10 variables that were most associated with I&D failure, and the predictive algorithm was built around those variables. In tests of its use, the predictor tool effectively anticipated actual results. For instance, for patients predicted to have a 10 percent probability for failure, the actual failure rate was 11.1 percent; and for patients with a predicted failure rate of between 20 and 30 percent, the actual rate was 25 percent. The app has been incorporated into PJI-related calculator apps (ICMPHILLY) and websites used by physicians across the globe, such as **icmphilly.com**. ■

> **"Identifying risk factors for admission to the ICU following elective TJA may help surgeons risk stratify patients and allow for higher-risk surgeries to be performed in facilities where an ICU is available."**
>
> Javad Parvizi, MD

Sending Jefferson Research to Space

Three of Jefferson's collaborative research projects will become part of the upcoming Rakia space mission, the first-ever private mission to the International Space Station. Scheduled for early 2022, Rakia will include 44 research projects to help scientists explore topics including the effects of low-gravity and space travel on the human body.

"The Rakia mission selected all three of the projects submitted by Jefferson and its institutional collaborators—Sheba Medical Center, the Ramon Foundation and the Israeli Space Agency at the Ministry of Science and Technology," explains **Zvi Grunwald, MD**, James D. Wentzler Professor of Anesthesiology and executive director of the Jefferson Israel Center, who helped foster the projects.

"These projects represent a great opportunity to learn about how life in space affects human health," says **Mark L. Tykocinski, PhD**, Jefferson provost and Anthony F. and Gertrude M. DePalma Dean of Sidney Kimmel Medical College. "More broadly, they reflect the innovation ethos that animates so many of our researchers—as well as the success of Jefferson's expanding global engagement."

One project, led by **Paul Chung, MD**, assistant professor of urology, will look at how low gravity and the space station environment might change an astronaut's urinary microbiome. "Urinary tract infection and urinary retention can be serious problems on space missions," says Dr. Chung. "Our project will assess the microbes in the urine before, during and after the space mission, to see how those microbes—both the good and the bad ones—change."

The project will have astronauts collect urine samples throughout the mission, and bring back samples for microbial analysis by next-gen sequencing. Collaborators also include **Javad Parvizi, MD**, clinical research professor and vice chair of orthopedic surgery, and researchers from Texas Tech University and Queen's University.

The laboratory of professor of neurology **George Brainard, PhD** is collaborating on a second project: This will monitor stress and sleep while testing stress interventions in novice space travelers. "For many years, our lab has been looking at how light can affect the human body, on Earth and in space. In fact, in earlier work, our lab built a full-sized replica of ISS crew quarters to study the effects of novel NASA light modules on sleep and the circadian system," says **John Hanifin, PhD**, assistant professor of neurology, who is leading the Brainard lab's contribution to this Rakia project.

The study will investigate how the stress of a space mission affects the human body, using visual, auditory and behavioral tests and electronic fit-bit-like wearables linked to mobile applications on Earth. As needed, the technology could help astronauts receive support from the ground.

In the third project, **Adam Dicker, MD**, professor and chair of radiation oncology, and colleagues, are collaborating on a study of the effects of space travel on immune dysfunction. Most astronauts suffer from changes in their immune system, including heightened immune reactions to reactivation of viruses that normally lay dormant in the body. The group aims to analyze the baseline immune state of astronauts using a sophisticated molecular analysis of more than 1,000 proteins from pre- and post-flight blood samples. ■

> **"These projects... reflect the innovation ethos that animates so many of our researchers—as well as the success of Jefferson's expanding global engagement."**
>
> Mark L. Tykocinski, MD

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