Thomas Jefferson University

RESEARCH

FUSING DISCOVERY, IMAGINATION and APPLICATION

IN THIS ISSUE

These 60 pages offer just a glimpse of the range and depth of studies undertaken across the Thomas Jefferson University research enterprise.

To learn more about Research at Jefferson, go to Jefferson.edu/Research2020.

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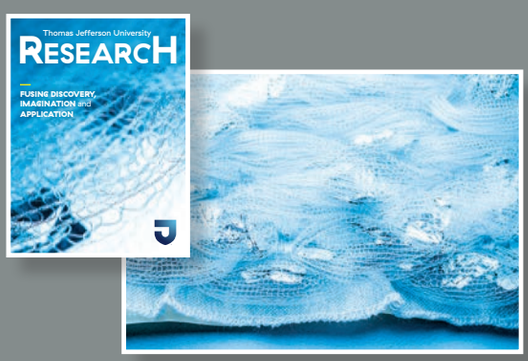
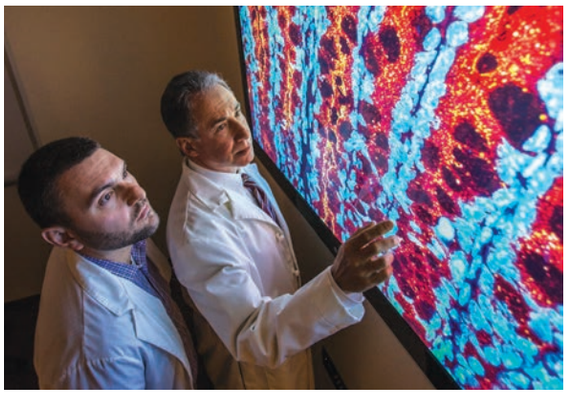
ON THE COVER



A CLOSER LOOK

Harnessing the power of macro lens photography, we are able to capture the detailed landscape of this textile designed by Jiyoung Park '19 as part of her MS in Textile Design thesis collection. The photograph next to the cover image above is a swatch sample of the exact same textile without magnification.



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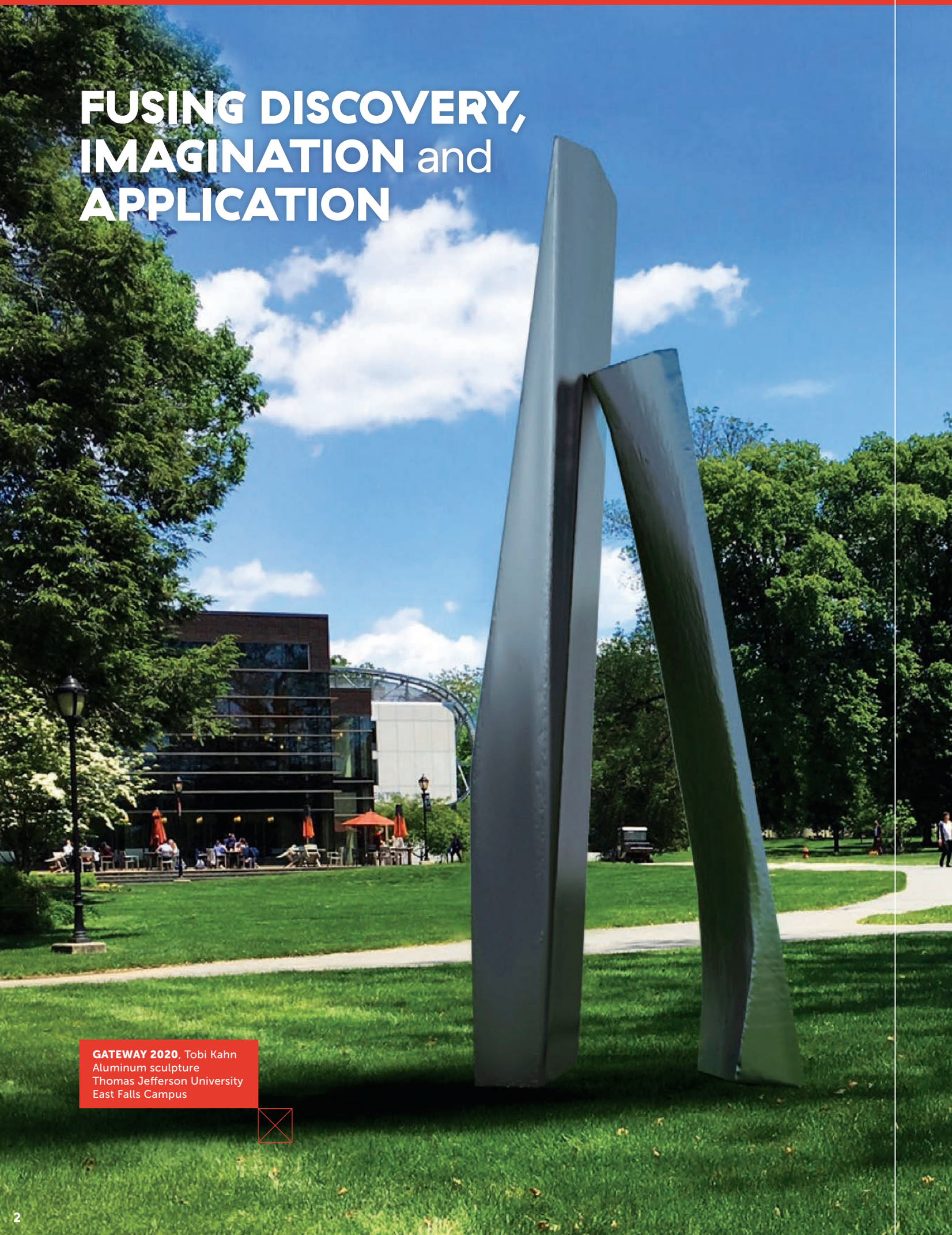
FUSING DISCOVERY, IMAGINATION and APPLICATION



GATEWAY 2020, Tobi Kahn
Aluminum sculpture
Thomas Jefferson University
East Falls Campus

THOMAS JEFFERSON UNIVERSITY IS A UNIQUE INSTITUTION, marked by dualities: simultaneously new and deeply experienced; steeped in tradition and heedless of traditional boundaries; professionally focused and committed to knowledge-creation.

We conduct research both for itself and as an essential part of the educational process. In doing so, we fuse discovery, imagination and application—weaving together the pursuit of basic knowledge with its innovative translation and creative application. We strive to redefine the term "humanly possible" in disciplines ranging from immunology and vaccine development to design and creation of functional fabrics.

New to the ranks of Carnegie Research 2 Doctoral Universities, Jefferson was born of two 19th century academic institutions long respected for education and research. We are committed to a full spectrum of research; and we have created a robust culture where impassioned faculty, students, clinicians and technical staff collaborate across the traditional divides between basic, translational, clinical and applied. We honor both sides of Abraham Flexner's assertion of the "usefulness of useless knowledge" by pursuing knowledge for its own sake and strategically mining practical impact (and human benefit) from what we learn.

From 1824 to Today

Thomas Jefferson University traces its roots to the 1824 founding of Jefferson Medical College. A pioneer in medical education, it was the first school where medical students learned by observing experienced doctors treating patients and, then, by participating in supervised, hands-on care. Since then, Jefferson researchers have had a record of discovery and research leadership in biomedical science and clinical care; and the University's research enterprise now includes a health system with nearly four million in- and out-patient visits a year.

In 2017, Jefferson joined with Philadelphia University to form a globally engaged professional university. Philadelphia University, founded in 1884, excelled at training professionals for careers in textile and material sciences, industrial design, architecture and health professions. A leader in hands-on professional education—exemplified by its pioneering "Nexus Learning™" model—it employed applied research to connect students and faculty with public and private organizations seeking solutions for practical, real-world challenges. Today, companies, nonprofits and government agencies—from Johnson & Johnson and Federal-Mogul to NASA and Oak Ridge National Laboratories—seek out the creativity and expertise embodied in the research and education programs that are Philadelphia University's legacy.

On that substantial cornerstone, we are building an even more robust research enterprise. We have, for example, established a new seed-funding mechanism (the Deans' Transformational Science Awards) and

a bridge-funding program to address unanticipated gaps in external grant support. We added staff to reduce investigators' administrative burden and facilitate collaboration across research groups and disciplines. And we launched new research and development platforms such as the Jefferson Institute for Bioprocessing (described on page 20).

Driving Forward, Strategically

If we are aggressive in building our research capacities and platforms, we are highly disciplined in our overall research strategy: identifying areas of strength and meaningful opportunity, and building programs that emphasize collaborative, transdisciplinary and cross-professional approaches. This strategy is most evident in our Programmatic Research initiatives, which aim to make rapid and meaningful advances in understanding complex diseases and major societal challenges. Programmatic initiatives comprise teams of researchers with distinct, complementary expertise, who pursue a cohesive set of projects that often extends from basic research to translational, clinical and applied. In this report, we feature several of those Programs—ranging from RNA Biology (page 38) and Fibrotic Diseases (page 46) to the creation of 21st century smart cities (page 32).

The best current example of Programmatic research's ability to drive rapid and meaningful advances is highlighted on page 18: our Vaccine Center's development of a COVID-19 vaccine candidate (CORAVAX™), which went into animal trials in March 2020.

At the same time, Jefferson is dedicated to supporting fundamental research on the most basic questions of science, engineering and society—studies driven not by institutional strategy but by investigators' passions to explore very specific questions and follow the answers wherever they lead. This report illustrates the array of basic research studies we are pursuing—on topics ranging from mitochondrial function (page 56) to the epigenetics of lung disease (page 48) and the molecular basis of uveal melanoma (page 11)—and it highlights how integral they are to both the pursuit of new knowledge and the discovery of solutions to specific challenges.

This report illustrates, too, the many ways that Jefferson investigators are pioneering in the application of new knowledge. From our clinical research on reducing surgical infections (page 54) and treating liver disease (page 42) to our applied research and development projects—in fields such as functional fabrics (page 50); medical and industrial

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. Many of the faculty members highlighted in this publication are affiliated with one or more of these research engines—powerhouses of discovery such as:

- 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.
- **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 airway disease, pulmonary fibrosis, pulmonary hypertension, lung inflammation and tobacco-related disorders. ■

THE EPISTEMOLOGY of JEFFERSON RESEARCH

Research at Jefferson falls into three not-mutually-exclusive categories:

- **Basic/Discovery Research**, which uncovers fundamental new knowledge in the sciences, engineering, social sciences and humanities.
- **Clinical/Translational Research**, which tests whether and how fundamental new knowledge can be translated for use—for example, in the clinical trial of a new drug.
- **Applied Research**, which subjects existing knowledge to new processes and technologies, and uses it to address specific needs for individuals, communities or organizations. It is the reduction-to-practice of prior research.

This way of organizing knowledge follows the conceptual model of scholarship presented in the 1990 Carnegie Foundation report Scholarship Reconsidered. The model comprises three interacting types of scholarship that, together, define a flexible approach that can apply to any discipline or professional field: Scholarship of Discovery, the commitment to knowledge for its own sake; Scholarship of Integration, which places special knowledge in a larger context; and Scholarship of Application, where knowledge is employed to address consequential human issues and often engages external clients.

Virtually all of research at Jefferson—from Basic/Discovery to Clinical/Translational to Applied—is grounded in or influenced by all three Scholarship lenses. This works because of the nature and range of professional and scholarly disciplines the University encompasses, and because of its determination to build transdisciplinary connections across the research spectrum. As you read this report, you will note that each article includes the appropriate category or categories to identify where the subject falls in the epistemology. ■

use of hemp (page 14); and the design of lighting for population health (page 28)—we are putting new knowledge to use, expeditiously, efficiently and productively to address real-world problems.

Overall, this document offers just a sample of the exciting work we have undertaken in pursuit of Jefferson's research mission:

Advancing and applying knowledge to improve lives.

These pages reflect the tremendous level of commitment, energy and momentum embodied in the Jefferson research enterprise. And they convey how proud—and ready—we are to join our Carnegie Research 2 Doctoral University peers in helping to define the future. ■

Mark L. Tykocinski, MD
Provost, Executive Vice President
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BASIC // DISCOVERY + CLINICAL // TRANSLATIONAL

ADVANCING CELLULAR and IMMUNE-BASED CANCER THERAPIES

Scott Waldman, MD, PhD and Adam Snook, PhD are developing a vaccine to fight colorectal cancer.

THE NCI-DESIGNATED SIDNEY KIMMEL CANCER CENTER (SKCC) is the heart of Jefferson's broad-based cancer research program. SKCC investigators are currently pursuing hundreds of basic science, translational and clinical studies on cancer cell biology and signaling, molecular biology and genetics, and specific diseases ranging from brain cancer to uveal melanoma. Among the most exciting efforts are partnerships between SKCC basic scientists and clinician-researchers to both advance new immune-based therapies and continuously improve current approaches.

Glioblastomas are aggressive brain tumors—and very hard to eliminate completely. However, a glioblastoma combination immunomodulatory vaccine approach developed by Jefferson researchers is now progressing into a phase II trial. The immunomodulatory vaccine product is notable for its initial success with a tumor type where previous immunotherapy approaches have failed.

Created by **David Andrews, MD**, professor of neurosurgery, and **D. Craig Hooper, PhD**, professor of cancer biology, the vaccine employs a patient's own tumor cells collected during surgical removal of the primary brain tumor. The researchers treat those cells with an antisense oligodeoxynucleotide (AS-ODN) containing immunostimulatory motifs. The AS-ODN works against a receptor shown to drive tumor growth and metastasis and the activity of tumor-promoting, anti-inflammatory macrophages. Next, the cells are loaded into a dime-sized diffusion chamber with additional AS-ODN, and the contents are irradiated. The chamber is then implanted under the patient's skin, allowing antigens produced by the cells and the AS-ODN to diffuse into the body to stimulate pro-inflammatory tumor-immune cells and boost anti-tumor immunity.

New Colorectal Cancer Vaccine

A new Jefferson-developed colorectal cancer vaccine also shows great promise. The adenovirus vector vaccine works by prompting an immune response specifically to a colorectal cancer tumor antigen called guanylyl cyclase (GUCY2C), first identified by **Scott Waldman, MD, PhD**, Samuel M.V. Hamilton Professor of Medicine. Developed by Dr. Waldman and **Adam Snook, PhD**, assistant professor of pharmacology and experimental therapeutics, the vaccine combines a GUCY2C molecule with a molecule that boosts the anti-tumor activity of CD8 positive cytolytic T lymphocytes. GUCY2C is expressed by cells lining the intestine and by at least several types of cancer cells; but, because the vaccine is injected into arm muscle, it does not come into contact with healthy intestinal cells.

In a phase I clinical trial, patients' blood showed markers of immune activation, suggesting that the vaccine could train the immune system to attack colon cancer cells that had spread before surgical removal. In pre-clinical mouse studies, the vaccine reduced the formation of colon cancer metastases in the lungs by >99% percent and more than doubled survival time. The researchers—who are preparing for phase II trials of the vaccine—recently found that GUCY2C is also expressed by gastric, esophageal and pancreatic cancer cells. They will pursue opportunities to test the vaccine with those cancers as well.

GUCY2C is also the target of a new CAR-T-based immunotherapy for colorectal cancer that Drs. Snook and Waldman have developed. The therapy—which engineers and re-infuses patients' own immune cells to target only the tumor—is preparing to enter phase I trials. Previously, a human-ready version of the therapy proved successful in killing tumors and preventing metastatic growth in mice—more than quintupling survival in cases with advanced lung metastases. Notably, there were no off-target or adverse effects of the treatment, which has been a major problem for other CAR-T cancer therapies.

Two–Step Approach

A unique approach to bone marrow transplant (BMT) involving half-matched (haploidentical) donors and higher-risk patients has proven as effective as transplants that use traditional, fully-matched donors. And continuing improvements in the procedure are driving even better results for patients. The "two-step approach"—developed by **Neal Flomenberg, MD**, professor of medical oncology—has been used in more than 300 procedures involving half-matched donors since 2006. Until recently, Jefferson was the only institution in the nation using the two-step approach.

In traditional BMT, chemotherapy (and, sometimes, radiation therapy) is administered before the patient receives an infusion containing both T-cells and stem cells in a single step; then immunosuppressive drugs are used to prevent or limit the otherwise overwhelming immune response that results in graft-versus-host disease (GVHD). In the two-step approach, after half the chemotherapy is administered, just donor T-cells are infused; two days later, the remaining chemotherapy is administered. (As a result, the cells spurring GVHD are eliminated, which lessens the need for a close HLA match.) Finally, an infusion of highly purified stem cells is given.

The two-step approach's benefits for patients are significant: less-aggressive regimes of immune-suppressant drugs; reduced incidence of GVHD; and engraftment of donor cells that occurs more quickly than with a traditional approach. Perhaps most significantly, the process and time needed to find a donor are reduced—a huge factor since approximately only 30 percent of patients will have a family member who is a full match. In addition, Dr. Flomenberg's approach gathers donor cells differently: rather than extracting stem cells from bone marrow, they are harvested from the donor's blood. It is less painful and less risky for donors, and enables the physicians to better standardize the number of cancer-fighting T-cells and stem cells (which replenish depleted blood supply) given the patient. ■

The glioblastoma and colorectal cancer vaccines reflect one facet of Jefferson's expansive basic science and translational research on vaccines. See *Vaccines Fighting Viruses and Cancer* on page 18 for a broader look at that work.

CLINICAL//TRANSLATIONAL

REAL WORLD DATA REVIEW SHEDS LIGHT on MEDICAL TREATMENT

In the largest population-based retrospective study on combination therapies for high-risk prostate cancer, a team led by **Grace Lu-Yao, PhD, MPH**, professor and vice chair of medical oncology, found that more patients live longer if treated with prostate removal (prostatectomy) plus radiation therapy. The study was the first to show that removing the whole prostate and following up with radiation therapy is associated with greater overall survival than simply treating the prostate with radiation plus hormone-blocking therapy.

"Prostatectomy is an unpopular treatment," notes Dr. Lu-Yao, whose research findings on cancer surveillance, screening and treatment for prostate cancer provide critical data for treatment decisions that improve patient care while reducing healthcare costs. "Our study showed that only six percent of men with high-risk cancer were treated with it. However, we found that 10 years after treatment, 89 percent of those who had prostate removal plus radiation were still alive—compared with 74 percent of those who received only radiation and hormone therapy."

Yet there were trade-offs for the survival advantages: Men who received prostatectomy and radiotherapy had increased rates of erectile dysfunction and notably higher rates of urinary incontinence. "One of the strengths of population-based studies is that they reveal what happens in the real world, rather than the carefully controlled context of a clinical trial," says Dr. Lu-Yao. ■


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Ten years after treatment, 89 percent of those who had prostate removal plus radiation were still alive.
Grace Lu-Yao, PhD, MPH
Professor and Vice Chair
of Medical Oncology

Elda Grabocka, PhD
Assistant Professor of
Cancer Biology and Surgery

BASIC// DISCOVERY

HOW to RE-STRESS PANCREATIC CANCER

WHAT IS THE MOLECULAR BASIS FOR PANCREATIC CANCER'S aggressive nature and resistance to treatment? **Elda Grabocka, PhD**, assistant professor of cancer biology and surgery, is working to find out. Last year, she received both a Margaret Q. Landenberger Research Foundation grant—which supports promising early-stage medical researchers—and her first NIH/NCI R01 grant. She has also received a V Foundation Scholar Research Award and a W.W. Smith Charitable Foundation grant. Her research investigates pancreatic cancer's ability to hijack the mechanisms by which normal cells adapt stressors. Ratcheting up that mechanism allows tumors to grow under adverse conditions and it enhances their resistance to chemotherapy.

Ninety percent of pancreatic cancers are associated with a mutation in the KRAS gene (one of the category of genes that are associated with 30 percent of all cancers). Dr. Grabocka's lab has identified that mutant KRAS cancers increase the activity of cell structures known as stress granules, which has the effect of enhancing tumor cell fitness and protecting it from chemotherapeutic agents. Dr. Grabocka and colleagues also developed methods that enable researchers to more effectively determine how stress granules are formed and how they support the development of pancreatic tumors.

Building on these initial discoveries, Dr. Grabocka is now using 3D cell culture models and mouse models to study stress granules' specific role in drug resistance and to investigate how oncogenic signaling and stress stimuli interact to promote pancreatic tumor development. Ultimately, she aims to develop strategies for targeting stress granules in treatments for a range of RAS gene cancers. ■

BASIC// DISCOVERY

CAN a PRIMROSE COMPOUND FIGHT UVEAL MELANOMA?

UVEAL MELANOMA IS THE MOST COMMON EYE CANCER IN adults. It metastasizes to the liver in 50 percent of patients, and there are no effective therapies to treat those metastases. Yet.

Jeffrey L. Benovic, PhD, Thomas Eakins Endowed Professor of Biochemistry and Molecular Biology, is globally recognized for research uncovering the mechanisms of G protein-coupled receptor (GPCR) signaling and how GPCR dysregulation contributes to disease. GPCRs regulate a variety of biological functions—from neurotransmission and sensory perception to the movement of cells in response to chemical stimuli. They have also been implicated in diseases ranging from cancer to neurological disorders.

GPCRs are the target of about 35 percent of drugs currently on the market—including those to treat cancer, cardiovascular and airway disease, and neurological and metabolic disorders. Dr. Benovic's broad-ranging work on the regulation of GPCR function is creating opportunities to improve on those therapeutics. He is often a catalyst for translational projects, collaborating with clinician-researchers to create and test new treatments for a variety of diseases.

Dr. Benovic and his colleagues recently identified a compound derived from a type of primrose that could be a potent inhibitor of metastatic growth in uveal melanoma. It works by blocking a particular type of G protein that sits on the cell membrane. In uveal melanoma, a subset of these G proteins are mutated, turning on a molecular pathway that leads the cell to become malignant. When Benovic lab researchers treated uveal melanoma cells with small amounts of the compound, the cells appeared to revert to their normal, non-malignant state. And higher doses killed the cells outright.

The next step: Dr. Benovic will work to confirm the findings in a mouse model of uveal melanoma, collaborating with **Takami Sato, MD, PhD**, K. Hasumi Endowed Professor of Medical Oncology, who directs **Jefferson's Metastatic Uveal Melanoma Program**—one of the nation's only centers dedicated to both research and treatment of the disease. ■

CLINICAL // TRANSLATIONAL

A NEW LOOK at CANCER CARE DISPARITIES

THE DEATH RATE FROM CANCER IS NOTABLY HIGHER FOR AFRICAN Americans than Caucasians, which derives from disparities in screening, diagnosis, engagement in clinical trials and therapeutic efficacy and less use of hospice and palliative care among African Americans.

"The causes of these complex disparities reflect social, cultural and economic inequalities more than biological differences," says **Lisa Whitfield-Harris, PhD, MSN, MBA**, assistant professor of nursing. "Addressing them effectively will require interventions that are developed in full partnership with the African American community."

She and two Jefferson colleagues—**Clara Granda-Cameron, DrNP, MSN**, assistant professor of nursing, and **Jeannette Kates, PhD, CRNP**, assistant professor of nursing and director of the adult-gerontology primary care nurse practitioner program—are collaborating on two studies that seek to clarify and begin addressing culturally based reasons for cancer care disparities within the African American population.

Promoting African American Engagement in Clinical Trials

The first study seeks to address the fact that—despite researchers' increasing efforts over the past 25 years—African Americans continue to be underrepresented in clinical trials. This underrepresentation means that trial results often do not accurately gauge a treatment's effectiveness for African Americans.

"Through this project, called **Empowerment Through Engagement: African Americans as Partners in Clinical Trials**, we will develop a culturally sensitive teaching tool to promote African

LEFT TO RIGHT: Yvonne Florence, Sisters R Us Circle of Survivors; Jeannette Kates, PhD, CRNP; Clara Granda-Cameron, DrNP, MSN; Lisa Whitfield-Harris, PhD, MSN, MBA

American community advocacy and engagement in clinical trials," says Dr. Granda-Cameron.

The study is a partnership between the Jefferson researchers and the cancer survivors' organization, Sisters R Us Circle of Survivors. It will use a community-based participatory research design and Freire's dialogue approach to explore participants' perceptions about participating in clinical trials, as well as concepts of racism, discrimination, resiliency and protective factors. The results will then be employed as the basis for collaborative development of the teaching tool.

Advance Care Planning among African Americans Diagnosed with Cancer

The second project explores perceptions of advance care planning among African Americans who have been diagnosed with cancer. "There is consistent evidence that African Americans are less likely to engage in goals-of-care discussions, complete advance directives or enroll in hospice or palliative care," says Dr. Kates.

Funded by a research grant from the provost's office, the project is using three structured instruments and follow-up conversations to measure and understand mistrust, decisional control preference and advance care planning readiness among study participants.

"Our goal is to use the information we gather in this study to create a culturally sensitive and highly effective intervention that helps increase the number of African Americans who engage in advance cancer care planning," explains Dr. Kates. ■

APPLIED //

REDISCOVERING HEMP:

New Materials, Manufactured Products and Therapeutics

THROUGH MUCH OF RECORDED HISTORY, THE HEMP PLANT was recognized as a sustainable, renewable resource with myriad practical applications. Its fibers are strong, resilient and possess unique chemical properties; its seeds and leaves are nutritious; and parts of the plant have medicinal benefits. However, for more than 50 years, its use in the United States was severely restricted by policymakers who equated all hemp products with just one: marijuana.

That situation has changed over the past decade. Today, most restrictions on hemp have been lifted, and states are legalizing marijuana and its by-products for medicinal or recreational purposes. That evolution has been driven by three factors: growing consumer demand for products created from renewable resources; better understanding of the hemp plant's complete physical and chemical composition; and expanding awareness of the known and potential medical uses of cannabinoids (including the fact that the human body not only uses cannabinoids but also manufactures its own).

Ron Kander, PhD, and student Natalie Burgos combine hemp hurd with biodegradable polymers in a laboratory-scale ejection molding machine to make hemp-reinforced polymer composites.

Mark Sunderland '84, M'06, and Michael Savarie '19 are evaluating material properties of Nano-film made from hemp flower extract to determine bio-test sequencing.

The basic and applied research associated with the engineered industrial and consumer products of the hemp initiative has been strategically guided by **Ronald Kander, PhD**, Executive Dean of Kanbar College of Design, Engineering and Commerce, whose research focuses include composite materials and sustainable manufacturing processes. "Since 2017," explains Dr. Kander, "Jefferson researchers have been pursuing four integrated goals: advancing basic scientific knowledge about hemp and its components; exploring where hemp could be a cheaper or more effective raw material for existing products; conceiving and creating wholly new biomedical and manufactured products; and defining markets and sustainable supply chains for those products."

Toward those goals, Jefferson's hemp-focused research ranges from basic and translational science and clinical trials to industry-sponsored ideation and product development. It engages dozens of departments across the University, from engineering and textile design to chemistry and surgery. Here we highlight two facets of the growing program.

Jefferson's hemp-focused research ranges from basic and translational science and clinical trials to industry-sponsored ideation and product development.

Manufactured Hemp

A collaborative research and development team—including Dr. Kander; **Mark Sunderland, MS**, Robert J. Reichlin High-Performance Apparel Chair; **Brian George, PhD**, associate professor of engineering and textile; and several colleagues—have been exploring and applying many of hemp's absorptive, antimicrobial, electrical and mechanical characteristics. The team's efforts have led to the development of a unique, environmentally sustainable method for processing hemp—one that creates new fibers and textiles using the whole plant—that could soon be the basis for an array of high-performance manufactured products with unique characteristics. Those products could include, for example, hospital gowns and working surfaces that are resistant to staph infection and the MRSA virus, and lighter, more durable yoga mats and blocks. One line of products is now being commercialized under the name Hemp Black.

Michael Leonard, MS Ed, MA Ed, Academic Dean of the School of Design and Engineering, is a scholar and practitioner of Industrial Design. He and his colleagues are guiding a broad array of student-driven research and development projects focused on hemp. Some concentrate on the development of consumer products, such as kitchen surfacing that leverages hemp's antimicrobial qualities, dog-calming chew toys made of CBD oil-infused hemp hurd (what remains after the fibers are removed from a stalk) or biodegradable 3D-printed seed starters. Dean Leonard and his colleagues are collaborating with a team led by non-woven materials expert Brian George. But they also explore the other end of the spectrum, asking questions such as, "Can we design equipment that reduces the steps involved in harvesting the plants and collecting their oils?"

Medicinal Cannabis

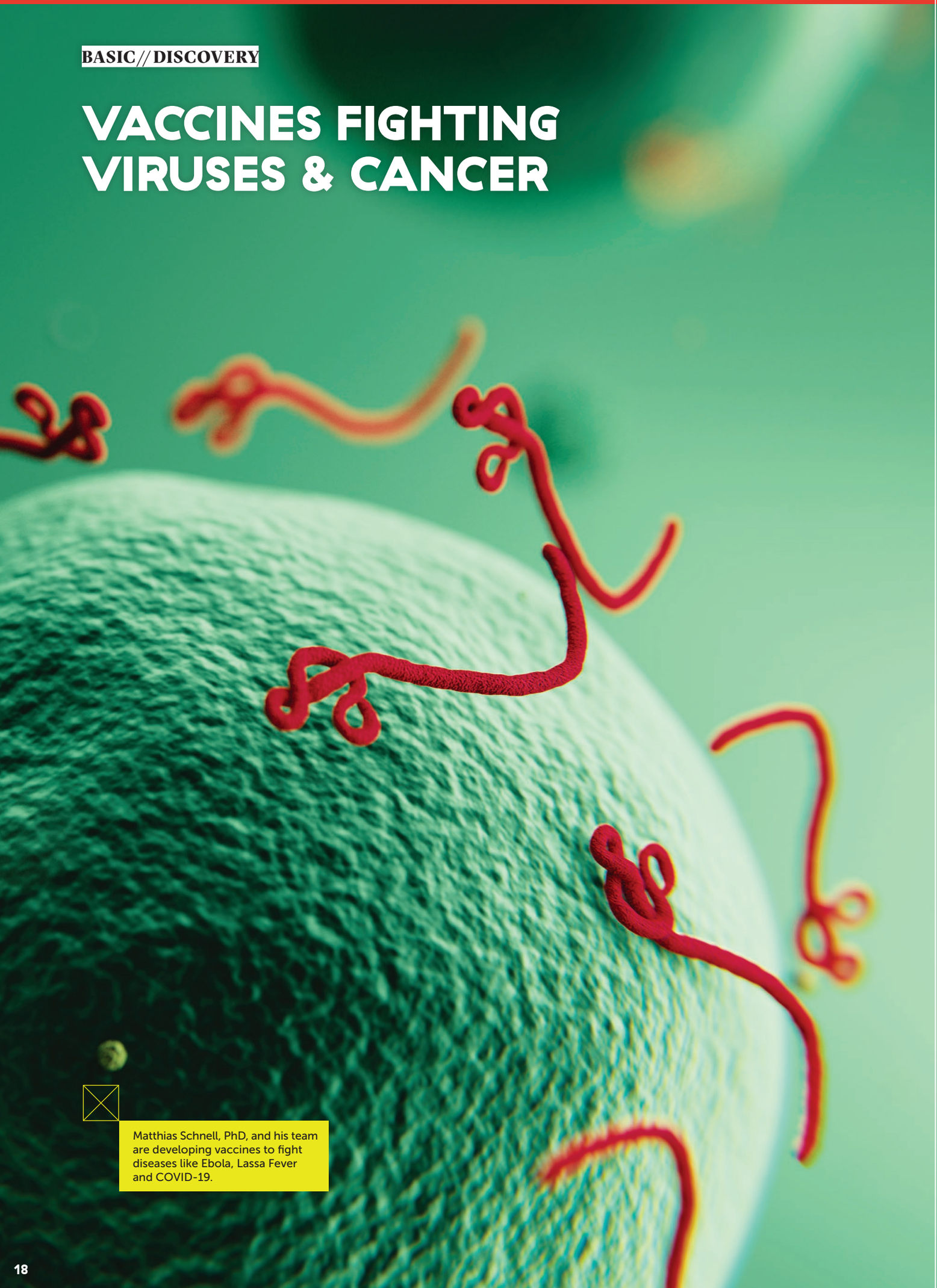
Jefferson's Lambert Center for the Study of Medicinal Cannabis and Hemp is a nexus for cross-disciplinary, multicenter and multinational research on the use of cannabinoid-based therapies. It also provides evidence-based information on medical uses of cannabinoid-based products to clinicians and patients. The Lambert Center provided support to Jefferson's hemp initiatives and is currently supporting several ongoing internal and external observational and pre-clinical research projects. Future plans include supporting more extensive research projects, with several already under development.

The Lambert Center and the **Institute for Emerging Health Professions** (IEHP, which is housed in the Jefferson College of Health Professions) launched three online graduate certificate programs in Cannabis Medicine, Cannabinoid Pharmacology and Cannabinoid Chemistry and Toxicology. IEHP plans to develop one of the nation's first master's degrees in medicinal cannabis. In addition, the Center is working with researchers and clinicians across Jefferson on research projects addressing multiple areas, ranging from study design and development of clinical data to the impact of medicinal cannabis on key patient populations.

In parallel with those projects, the **Department of Rehabilitation Medicine** is pursuing two current studies. One project begins to address the dearth of evidence on the long-term effects of marijuana use by identifying health and functional variables that are most (and least) influenced. It will monitor physical health, cognitive function, quality of life and day-to-day function of three study groups: persons who currently use cannabis, those who used it previously but not currently, and those who never used it. Beyond the basic knowledge it will produce, the project will also provide a basis for outcome metrics that can be applied to clinical trials on cannabis-based therapeutics.

The second project addresses patients' perspectives, experiences and knowledge of cannabis. Among many uses, its findings will support development of patient and caregiver educational programs that counter broadly held inaccuracies. ■

VACCINES FIGHTING VIRUSES & CANCER



Matthias Schnell, PhD, and his team are developing vaccines to fight diseases like Ebola, Lassa Fever and COVID-19.

A GROUP OF JEFFERSON VIRAL VACCINE RESEARCHERS LED by **Jefferson Vaccine Center (JVC)** director and professor of microbiology and immunology **Matthias Schnell, PhD** have been using rabies vaccine as a potent tool for understanding and fighting hemorrhagic viruses—such as Ebola, Marburg, Sudan and Lassa Feve—as well as coronavirus. By the end of 2019, the team had developed a tetravalent vaccine that uses an established dead-virus rabies vaccine modified with specific antigens for the viruses. In animal models, the immune system develops a reaction to the vaccine that is specific and can defend against rabies and some viruses. Soon after COVID-19 first emerged, Schnell and his team created a killed-rabies vaccine that incorporates the spike portion of the SARS-COV-2 virus, which causes the disease. The resulting COVID-19 vaccine candidate—CORAVAX™—was put into animal trials as a prelude to expected phase 1 clinical trials.

The importance of leveraging our approach to create a coronavirus vaccine candidate is clear.

"Rabies is a prevalent problem in much of the world, and it is extremely hard to prevent spread of hemorrhagic viruses—evidenced by the most recent Ebola outbreak. It would be valuable to be able to provide immunity against these diseases simultaneously," Dr. Schnell says. "And the importance of leveraging our approach to create a coronavirus vaccine candidate is clear."

The NIH-funded project involves a bench-to-bedside range of work: From identifying and applying the antigens and observing the quality of the antibody response to developing a scalable production process to planning clinical trials. With the vaccine having proved effective and safe in small and large animal models, Dr. Schnell's team is working with a production facility to ensure Good Manufacturing Processes of the vaccine formulation. That process, which should be completed in the coming year, will be prelude to a subsequent phase I clinical trial testing toxicity. If early clinical trials are successful, the vaccine could be ready to test in actual disease outbreaks within five years.

JVC is the cornerstone of the University's programmatic research in immunology and infection disease. Building on basic and translational studies in immunology, microbial pathogenesis and tumor immunology, JVC researchers pursue multifaceted investigations on vaccines that combat viruses and those that provoke immune response to diseases such as cancer.

JVC researchers are also seeing robust results from their rabies-based vaccine for Nipah virus, which is transmitted from animals to humans and causes severe respiratory illness that can progress into encephalitis, seizure and coma. Outbreaks have occurred in Malaysia, Singapore, Bangladesh and India; and because no vaccine is available, the World Health Organization has listed Nipah as needing urgent action. A recent study in mice—testing a rabies vector that incorporates a Nipah virus gene—showed that one dose of the vaccine was safe and elicited strong antibodies response against both Nipah and rabies. A second, chemically killed version of the vaccine—which could be ideal for immunocompromised individuals—also safely induced strong immunity.

Rabies' unique method for attacking the brain—it bypasses the blood system and the blood-brain barrier by entering the central nervous system (CNS) through muscles at the site of an infecting bite—makes it a perfect tool to learn about ways of harnessing the power of the immune system to fight tumors in the brain. Results from recent studies by JVC investigators found that delivering rabies vaccine through a mouse's jaw muscles promoted an immune response in the brain—one sufficient to prompt CNS immune memory and protect against rabies in a way current vaccines do not. The study also demonstrated that for immune mechanisms to properly protect the brain long-term, immune "memory" cells must become resident in the CNS. That suggests immunity established in the blood is insufficient to fight brain cancer—a potentially pivotal finding for development of vaccines against the disease.

That study was one in a series of projects in which Jefferson researchers are translating their basic science discoveries into immune-based cancer treatments that have proven effective in early trials. See *Advancing Cellular and Immune-based Cancer Therapies* on page 6 for a look at that work. ■

JEFFERSON INSTITUTE for BIOPROCESSING:

Advancing Biologics R&D

A JIB employee sets up a 2 L bench scale bioreactor for CHO cell culture.

BELOW: JIB is the kind of facility you see in a manufacturing setting—and it is unique among academic institutions.

JIB will help **advance research** and development of biologics, supporting both academia and industry.

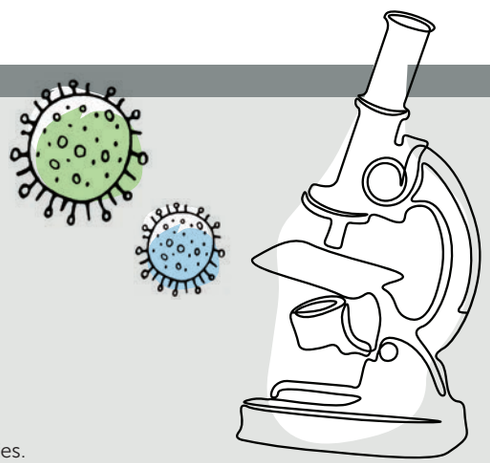
BIOLOGICS REPRESENT ABOUT 40 PERCENT OF DRUGS IN THE therapeutics development pipeline, and currently account for more than $200 billion in annual global revenue. It is an area primed for extraordinary growth. But research and development by pharmaceutical companies and manufacturers—and academic research centers—are limited by the lack of trained professionals in this field.

To meet these critical workforce needs, Jefferson established **Jefferson Institute for Bioprocessing (JIB)**. It is the first—and only—specialized education and training institute for biopharmaceutical processing in North America that combines commercial single-use processing equipment with a curriculum created in collaboration with the Ireland-based National Institute for Bioprocessing Research and Training (a joint effort of University College Dublin, Trinity College Dublin, Dublin City University and the Institute of Technology, Sligo). JIB—which opened its 25,000 square foot training and education facility in May 2019—provides training to industry professionals through workshops and certificate programs and hands-on education of new bioprocessing engineers at the undergraduate and graduate levels. "This is the kind of facility you see in a manufacturing setting," says **Parviz Shamlou, PhD**, JIB's executive director. "It is, we believe, unique among academic institutions."

Different Manufacturing Process Means Challenges

The growth of biologics represents a major industry shift from traditional chemical synthesis techniques. Biologic pharmaceuticals are manufactured in a living system, such as a microorganism, plant or animal cell, often using recombinant DNA technology. However, with a complex manufacturing process and lengthier regulatory approval process compared to traditional small-molecule drugs, biologics remain challenging to produce.

"Biomanufacturing is going through an unprecedented period of innovation in new products and growth in legacy therapeutics," says Dr. Shamlou. "JIB will help advance research and development of biologics, supporting both academia and industry." ■



CLINICAL // TRANSLATIONAL

PUBLIC HEALTH STUDY AIMS to INCREASE HPV VACCINATIONS

Too often, cultural, educational and demographic barriers hamper the public's use of vaccines. Among the most prominent examples is the human papillomavirus vaccine (HPV): roughly half of U.S. adolescents are not vaccinated and remain vulnerable to the virus and the cancers it causes.

"You'd have a hard time finding a parent who doesn't want to protect their child from cancer," observes **Amy Leader, DrPH, MPH**, associate professor of population science. "Still, many parents are missing an opportunity to protect their children from HPV, the most common sexually transmitted infection and a leading cause of cancers."

Dr. Leader is deeply engaged in developing and studying new approaches to increase HPV vaccination rates among high-risk populations. She and her colleagues recently completed an NIH-funded study on strategies to increase HPV vaccination rates among vulnerable populations in the Philadelphia region.

The study had three aims. The first sought to identify barriers to HPV vaccination in Hispanic and African immigrant communities. The researchers found that, despite a high level of awareness of the HPV vaccine among the broader Philadelphia-area population, members of marginalized communities had much lower awareness of the vaccine's availability and effectiveness, and received far less information through media, community and public health channels.

The second aim used citywide vaccination records and data on social determinants of health to identify novel predictors of HPV vaccination; initial analyses suggest several predictors, including neighborhood-level economic stability.

The project's final aim sought to better understand the content and nature of public discourse about HPV vaccination on social media channels. The team found that anti-vaccine messaging was delivered most often—and very effectively—through narrative communication (in other words, storytelling). In contrast, pro-vaccine messaging tended to be built around objective data, which was less compelling to many audiences.

"The data suggests that public health messaging needs to be more engaging, more focused on telling people's stories than on conveying nuts-and-bolts facts," Leader notes. To test that hypothesis, she and her colleagues are undertaking an NIH-funded randomized controlled trial that uses Twitter to communicate either science-based content or narrative messages that prompt feelings of empathy, transportation, and identification. Subsequently, they will then track the rates of adolescent HPV vaccination. ■

STEM CELLS as a PATHWAY to NEURO REGENERATION

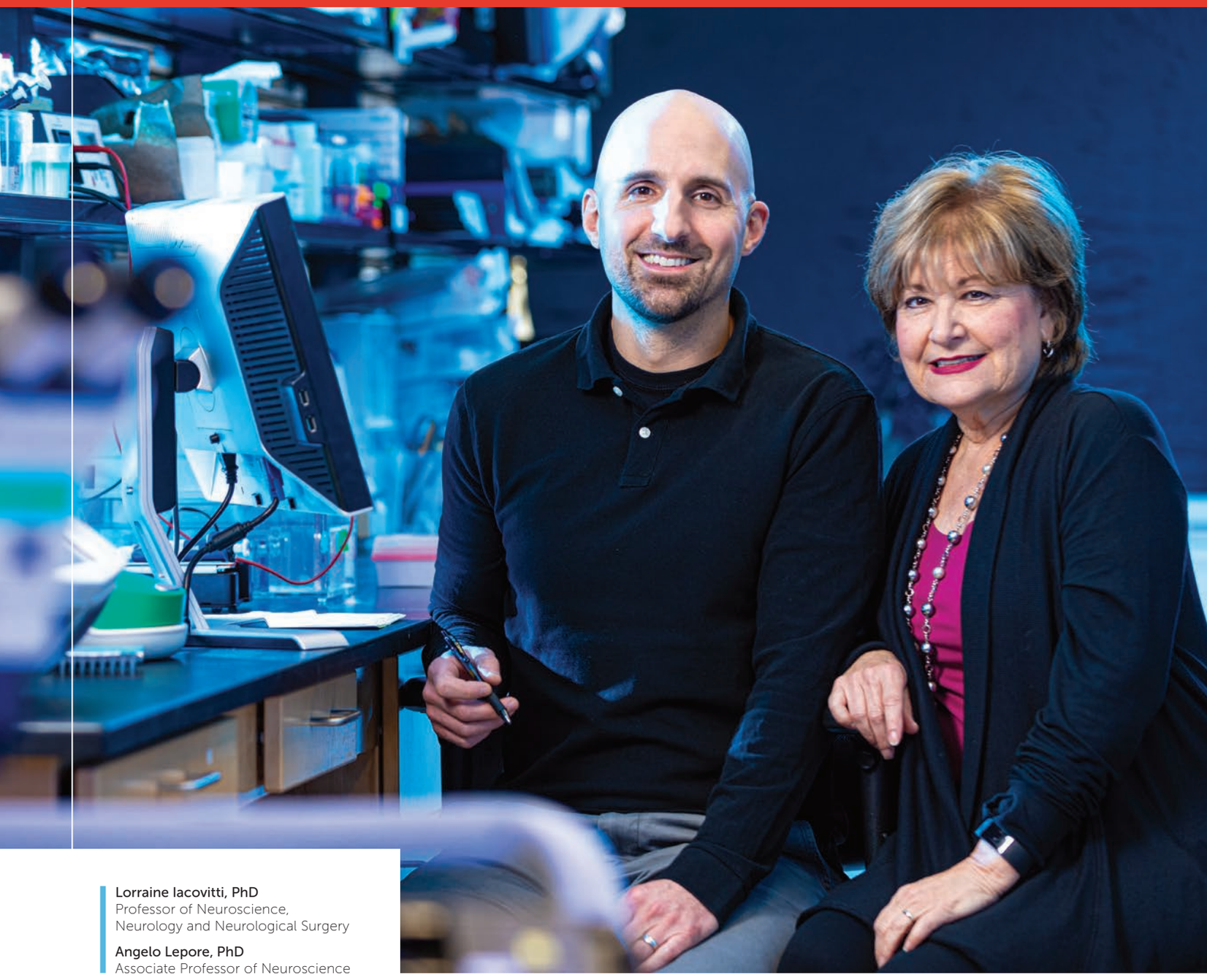
BIOSCIENTISTS' ABILITY TO CREATE INDUCED PLURIPOTENT stem cells—which can be differentiated into many kinds of cells has opened new pathways for research and treatment of many medical conditions. One of the most notable areas of advancement by stem cell researchers at Jefferson is in treatment for conditions affecting the central nervous system.

For more than 20 years, **Lorraine Iacovitti, PhD**, professor of neuroscience, neurology and neurological surgery, has been making major research contributions in stem cell biology and the use of induced pluripotent stem cells (iPSCs) to pursue therapies for stroke and neurodegenerative disease. Her breakthrough discovery for prompting stem cells to differentiate into dopamine neurons has overcome a major obstacle to using iPSCs therapeutically. More recently, in studying an animal model of stroke, she discovered the existence of stem cell niches in the brain, which means that new cells can be created throughout the adult brain. That work also showed a dramatic surge in stem cell proliferation and differentiation due to molecular and cellular changes in the blood-brain-barrier after stroke. Her lab is now pursuing opportunities to leverage these changes to deliver stem cell therapeutics.

Recently, Dr. Iacovitti has also identified distinct roles in Parkinson's disease played by nervous system cells called astrocytes. Parkinson's is characterized by degeneration of dopamine neurons in the substantia nigra region of the brain, while those of the neighboring ventral tegmental area (VTA) are relatively spared. In comparing the two regions, Dr. Iacovitti found that astrocytes in the VTA produce growth factor GDF-15, which can protect dopamine neurons from the disease. The findings suggest that microenvironments in the brain may play a significant role in neurons' susceptibility to neurodegenerative disease—and they raise the tantalizing possibility of a new Parkinson's therapy using patient-specific iPSC-derived VTA astrocytes.

Iacovitti's colleague, **Angelo Lepore, PhD**, associate professor of neuroscience, is also using iPSC-derived astrocytes, but for a different purpose: to study cellular mechanisms underlying traumatic spinal cord injury (SCI). He is particularly interested in understanding SCI-related respiratory dysfunction and chronic neuropathic pain; and he hopes to develop stem cell-based therapies that both address the primary injury and protect neurons during the period of secondary damage that patients experience. Toward that end, Dr. Lepore is working on several research paths involving astrocytes: identifying molecules that inhibit or promote regeneration of the axons that extend from nerve cells; uncover astrocytes' role in maintaining normal nervous system function; and to pinpoint how alterations in synapse signaling contribute to SCI disease processes.

It is known that, after SCI, astrocytes often lose the capacity to properly regulate glutamate in neuronal synapses, which contributes to further neurological damage. Dr. Lepore's lab has demonstrated that



Lorraine Iacovitti, PhD
Professor of Neuroscience,
Neurology and Neurological Surgery

Angelo Lepore, PhD
Associate Professor of Neuroscience

transplanting iPSC-derived astrocyte progenitor cells can help protect respiratory function in animal models of SCI. Now they are doing the fundamental work necessary to demonstrate the potential of using patient-specific iPSC-derived astrocyte progenitor cells therapeutically.

Astrocytes also naturally promote growth of axons, which are long fibers that extend from neurons to convey electrical signals to other neurons and muscles—a significant fact, given that axons do not regenerate after central nervous system injury. Dr. Lepore and his colleagues are engaged in a long-term NIH-funded study of the role astrocytes might play in promoting of axon regeneration and sprouting to recovery of respiratory function following SCI. Thus far, using a rat model of SCI, the researchers have demonstrated that astrocyte stem cells transplanted at spinal injury sites promote robust axon growth and significant restoration of diaphragm function—by prompting regenerating axons to reconnect the neural circuit between brain, spine and diaphragm that regulates breathing. They have also found that astrocytes significantly dampen the pro-inflammatory response that promotes secondary damage. In their continuing work, they are selectively silencing defined neuronal populations involved in respiratory control, in order to understand which kinds of axon growth actually promote recovery of diaphragm function—information that will be essential to develop new therapies. ■

BASIC// DISCOVERY + CLINICAL// TRANSLATIONAL

TEAMING UP on AUTISM

AUTISM SPECTRUM DISORDER (ASD)—THE MOST COMMON neurodevelopment disorder of childhood—is characterized by challenges with social skills and communication, repetitive behaviors and sensory sensitivities.

The **Jefferson Autism Research Program** is comprised of a team investigating the molecular, genetic, synaptic and functional aspects of ASD. Program researchers and clinicians translate newly gained knowledge into treatments and behavioral interventions intended to improve the function and quality of life of those with ASD.

Roseann Schaaf, PhD, professor of occupational therapy, leads a multi-project study investigating ASD-associated sensory perception and integration difficulties. These often include hypersensitivity to sounds, sights and tactile sensations and trouble perceiving and integrating those sensory inputs—and can lead individuals with ASD to become overwhelmed and unresponsive. In addition, she is investigating whether occupational therapy designed to address ASD-related sensory challenges can create long-lasting improvements in everyday functional skills. Dr. Schaaf's lab is conducting a large, NIH-funded clinical trial of sensory integration interventions in collaboration with Albert Einstein Medical Center in New York. The project tracks both improvements in children's functional capacities and changes in their brains' neurological processing.

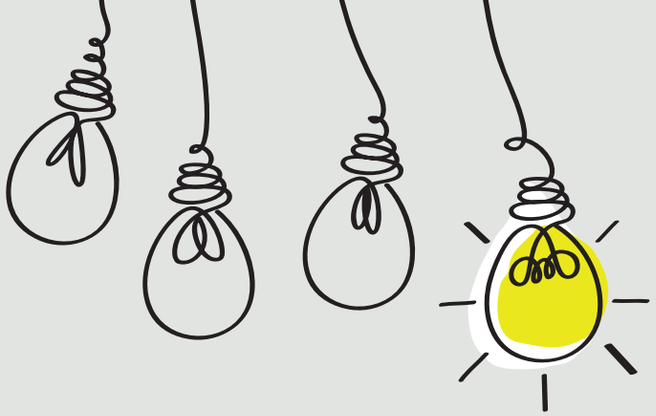
LEFT TO RIGHT: Matthew Dalva, PhD; Diane Merry, PhD; Roseann Schaaf, PhD; Judith Ross, MD

And she is developing and testing an assessment of sensory features in ASD, which should allow for more precise identification and treatment of an individual's sensory challenges.

ASD is more prevalent in males, but the reason is not clear. **Diane Merry, PhD**, professor of biochemistry and molecular biology, is working toward an answer by studying the basic biology of two proteins produced by sex-chromosome-linked genes. These proteins, which are critical to synapse formation and stabilization, have increased expression in boys with some types of ASD. For these studies, Dr. Merry is creating specialized lines of patient-derived stem cells, which can be turned into neurons in order to study the biochemical and functional characteristics of these synaptic proteins.

Mounting evidence indicates that ASD is a "synaptopathy"—a disease rooted in atypical function of the synapses through which brain neurons communicate. **Matthew Dalva, PhD**, professor of neuroscience, directs the Jefferson Synaptic Biology Center (SBC), which seeks to address how these building blocks of the brain form, function and are linked to disease. His laboratory uses leading-edge imaging and new molecular tools to study how synapses are made and lost, and what impact abnormal morphology and quantity of synapses have on brain function. Dr. Dalva's current studies address synaptic defects in ASD, but his work—and that of his SBC colleagues—will likely also shed light on a range of other neurological conditions including addiction, Alzheimer's and neurodegenerative disease.

Judith Ross, MD, professor of pediatrics, directs the Extraordinary Kids Clinic at Nemours/Alfred I. duPont Hospital for Children, which serves children with X and Y chromosome variations. She has more than 25 years of NIH-funded pediatric research experience focused on neurodevelopmental outcomes in children with X and Y chromosomal disorders such as XYY, Klinefelter and Turner syndromes. Her Jefferson lab applies that basic science expertise and her deep clinical experience to the challenge of uncovering ASD's genetic roots. ■



CLINICAL//TRANSLATIONAL

CAN WE TEACH CREATIVITY?

Creativity is an increasingly important skill for navigating the 21st century. But how do human beings acquire that skill? Can it be taught? **Richard W. Hass, PhD**, assistant professor of psychology, believes it can. "I want to understand the processes through which we solve problems creatively," he says, "and then use those processes as the basis for curricula that prepare students to hone creativity as a tool for managing life in a swiftly changing economy, society and environment."

Toward that ambitious goal, Dr. Hass is pursuing a broad range of interdisciplinary studies on the cognitive and social processes underlying creative thinking, conceptual combination and motivation. His collaborators include experts in philosophy, neuroscientists, anthropologists, statisticians and experts in educational assessment—from institutions around the globe, including University of Alberta, Canada, and The Free University of Berlin, Germany. Their projects include:

- studies on how memory search processes enable people to generate novel ideas;
- an investigation of the interplay of cognitive and motivational variables in predicting real-world creative achievement;
- the identification of common facets of human idea-generation and problem-solving processes—and comparison of those facets with artificial intelligence strategies;
- development of creativity measurement tools and assessments of how feedback affects the problem-solving process.

Applying Research to Curriculum Development

As the research produces concrete findings, Dr. Hass is applying them to curriculum development and to assessments of the classroom experience. With Jefferson colleagues, he is:

- helping to develop and pilot a creativity core curriculum for use across the university studying the correlation between teachers' beliefs about creativity generally and about teaching for creativity;
- working with the **Jefferson Center for Interprofessional Practice and Education** to perform statistical analysis on—and create outcomes-based assessments of—team-focused education.

"The curriculum we are developing will, we believe, help our graduates to creatively—and successfully—address challenges and tasks for which there is no single 'right' answer," Dr. Hass explains, "and to use what they know to confront situations involving outcomes that may be inherently unknowable." ■

CLINICAL//TRANSLATIONAL

INCREASED ACTIVITY MAY PREVENT COGNITIVE DECLINE

Participating in cognition-enhancing activities might reduce African Americans' risk for dementia.

AFRICAN AMERICANS ARE AT NEARLY TWICE THE RISK AS Caucasians for developing Alzheimer's and other dementias. Yet, no interventions have been shown to reduce this disparity.

Barry Rovner, MD, professor of psychiatry, neurology and ophthalmology, and a clinical expert in Alzheimer's disease, has been intensely studying racial-based disparities in the incidence and outcomes of dementia. In one notable study, he and **Robin Casten, PhD**, professor of psychiatry, found that African Americans were less likely than whites to recognize cognitive decline as a medical problem. Those findings suggested that culturally specific interventions might help reduce African Americans' risk for developing dementia.

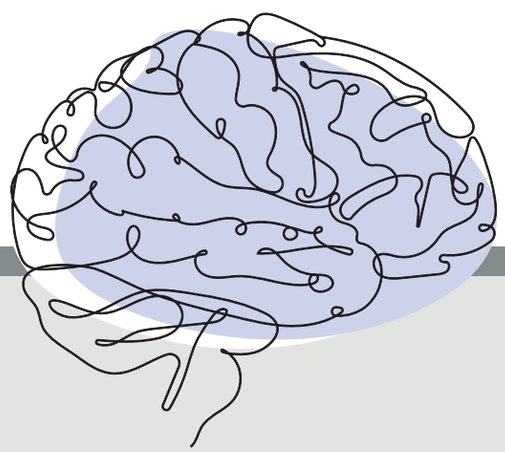
Therefore, Drs. Rovner and Casten undertook an NIH-funded trial of a behavioral intervention that increased participation in cognitive, physical and social activities among African Americans with mild cognitive impairment, a transition state between expected cognitive aging and dementia. In the intervention, community health workers used goal setting and action planning to guide at-risk participants in concrete steps to increase cognition-

enhancing activities. In results published last year, the research team reported that the intervention had clear benefit in helping prevent memory decline in this high-risk population. The behavioral intervention reduced risk of cognitive decline by 88 percent, compared to a control group.

Dr. Rovner attributes much of the intervention's success to the study's sensitivity to the perceptions of the African American participants. The community health workers were themselves African American, and the participants were able to self-select the specific activities they pursued—which included relearning chess, playing guitar, rejoining a church group, making plans to meet friends for lunch and walking to appointments.

While conducting the study, the researchers became more aware of the problems facing African Americans with diabetes—which can cause microvascular disease and neurodegeneration and, thereby, increase risk for dementia. The number of older African Americans with diabetes in the U.S. will double by 2030, and African Americans have worse glycemic control than Caucasians.

To address these disparities—and the related incidence of dementia—Drs. Rovner and Casten are planning a clinical trial on the Efficacy of Diabetes-Specific Behavioral Activation. The researchers hope that, by reinforcing diabetes self-care and addressing African Americans' negative beliefs about medications and physicians, the intervention will simultaneously improve diabetes care and prevent dementia in this high-risk population. ■



BASIC// DISCOVERY

EXCITING FINDINGS on EPILEPSY

Epilepsy, one of the most common neurological conditions, is characterized by recurrent seizures prompted by abnormal, excessively synchronous firing of neurons in the brain. It may be caused by abnormal brain connections, an imbalance of neurotransmitters or changes in signaling channels within brain cells. For about 70 percent of patients, seizures can be controlled with pharmaceutical treatments. But for many—especially those who experience prolonged seizures—current treatments are ineffective and epilepsy can be life-threatening.

Clinician-scientist **Michael Sperling, MD**, Baldwin Keyes Professor of Neurology, is internationally known for his work in epilepsy surgery and electrophysiology. He integrates clinical practice with research, trying to understand why certain patients benefit from available treatments—and to identify new, effective therapies for those who do not. Dr. Sperling founded and directs the **Jefferson Comprehensive Epilepsy Center**, noted for its basic science and clinical research on epilepsy's underlying mechanisms and on experimental therapeutics. Center researchers are using electrophysiology, structural MRI and functional MRI to map seizure spread within the brain, observe seizure effects on structures involved in cognition, memory and language and develop methods for preventing seizure onset.

Recently, Center researchers found that some seizures start after a burst from neurons that inhibit brain activity. In other words, neurons that dampen other neuronal activity may be key to starting the large-scale hypersynchrony that becomes a seizure. The study, which was part of the group's search for activation-and-resting patterns that correlate with more significant seizures, was the first time that the pre-seizure neural inhibition was seen in patients. In the study, performed in collaboration with neurosurgeons at Jefferson and University of California at Los Angeles, patients undergoing preparation for epilepsy surgery had electrodes placed in the brain to determine the exact location of seizure onset. The electrodes then captured signals from the individual excitatory and inhibitory neurons involved in the seizures. Analysis of cell signaling showed that inhibitory neurons fired immediately prior to the excessive discharge of excitatory neurons. This inhibitory burst may increase the likelihood of subsequent hypersynchronous firing that leads to a seizure.

Among the researchers' goals in leveraging these findings is to develop a way to use the pre-inhibition phenomenon as a biomarker for determining who will (and will not) respond to seizure-prevention therapy. Other biomarkers are also being investigated—in particular, functional MRI signals—in hopes of better predicting response to therapy and developing new methods of modifying abnormal neuronal firing. ■

LIGHT4HEALTH:

How Does Light Impact Health?

WE USE LIGHT TO CONTROL HOW WE PERCEIVE AND ENGAGE with environments in which we live, work and play. In turn, light affects our endocrine system and circadian rhythm and impacts our emotions, focus and performance. And the practical purposes to which we apply light are expanding dramatically. Light Research at Jefferson addresses a wide spectrum of questions on how we do—and could—use light, and how light affects human psychology and physiology. It includes both deep, field-specific investigations and interdisciplinary work engaging faculty from architecture and interior design to engineering and material science to basic bioscience and clinical care.

It also extends to education: Jefferson is a key partner in Light4Health, an international collaboration to develop an innovative health research-based academic curriculum in lighting design education. The project is underwritten by Erasmus+, the European Union's program that promotes infusion of research-based discovery back into education to address emerging societal needs. Jefferson's collaborators include universities in Denmark, England, Germany, Russia and Sweden.

Light4Health's researchers and design practitioners are developing a transdisciplinary curriculum on the intersection of lighting design and health research—integrating methods and tools from neurology, photobiology and neuroendocrinology, and findings from research in neurobehavior, psychophysiology of perception and behavioral, cognitive and environmental psychology.

Lyn Godley, associate professor of industrial design, is the project's principal investigator at Jefferson. She brings to bear both substantial design expertise and a talent for nurturing young designers—as well as a track record of developing innovative, cross-disciplinary curricula that link multiple design fields with business, engineering and science. Godley's key partner on the project is **George Brainard, PhD**, professor of neurology and widely respected director of Jefferson's Light Research Program—which, among its many projects, is working with NASA to develop and test lighting solutions to the disruption of sleep and circadian rhythms that astronauts experience during space flight. ■

Rowena McBeath, MD, PhD
Assistant Professor of
Orthopedic Surgery

BASIC// DISCOVERY

A KEY to PREVENTING TENDINOSIS

RESEARCHERS HAVE LONG KNOWN THAT WITH AGE, BLOOD supply to tendon cells decreases, leaving them starved of oxygen. But knowing why this occurs and why it causes tendons to fray with age can be critically important to creating treatments that eliminate the need for surgery for tendinosis, a painful orthopedic condition.

An intriguing NIH GEMSSTAR-funded study by **Rowena McBeath, MD, PhD**, assistant professor of orthopedic surgery, found that the paired reduction of oxygen supply and the signaling molecule Rac1 causes aged tendon cells to change shape and flexibility. The findings have broad implications for both injury prevention and tissue repair.

In Dr. McBeath's study, donated human tendon cells were grown in an environment mimicking the low-oxygen environment common in older people. Those cells changed shape and became round and more similar to tough cartilage-like cells; in addition, older tendon cells reduced their production of the signaling molecule Rac1, which helps govern cell shape movement, and growth. With reduced Rac1, the tendon cells began to change shape—but only in low-oxygen conditions.

Now, Dr. McBeath is exploring whether increased Rac1 production might enable tendon cells to keep their shape and thus prevent tendinosis and the associated pain. She and her team are also working in the opposite direction: studying the possibility of using decreased levels of oxygen and Rac1 to spur cells to become fibrocartilage. Success in that effort could ultimately give clinicians the ability to grow patient-specific tissues to replace damaged tissue in the knee, hip or spine—in the long term, potentially obviating the need for joint replacement surgery. Dr. McBeath's new work has also received NIH support through a five-year K76 Beeson Career Development Award. ■

CLINICAL // TRANSLATIONAL

IDENTIFYING BIOMARKERS to ASSESS PEDIATRIC SPINAL INJURY

DIAGNOSING AND ASSESSING SPINAL CORD INJURY (SCI) in children and adolescents has long been a challenging task, as has been the application of relevant and established outcomes measures for these patients. "In adults, the neurological consequence of SCI is determined by physically examining 56 sites on the patient's body—examinations that require full participation and cognitive awareness," explains **Mary Jane (MJ) Mulcahey, PhD**, professor of occupational therapy.

"But we showed in a study of 236 children with SCI that children younger than six years—and some up to 10 years old—are not able to participate effectively. The clinical assessment of SCI is also challenging with adults who have brain injury or are in a coma or medical-induced sedation. We need to develop imaging biomarkers that tell us—regardless of a patient's age or mental capacity—the precise extent of damage."

With a team of biostatisticians, engineers, neuro-radiologists, neuroscientists, occupational therapists and physicists, Dr. Mulcahey has been developing and validating spinal cord imaging biomarkers and testing the feasibility of neuroimaging to predict SCI outcomes. Their proof-of-concept study employed diffusion tensor imaging (DTI) to

MJ Mulcahey, PhD, met Miki Greenstein, pictured, soon after he had a spinal cord injury at the age of 13. She has worked with him for 20 years now, and he is a frequent participant in her research studies. Here, she and student Samantha Burke work with Miki on a SaeboReJoyce rehabilitation workstation that helps with arm and hand training.

> This work could fill a major gap in **pediatric care**.
>
> **Mary Jane Mulcahey, PhD**
> Professor of Occupational Therapy

effectively analyze both direct and indirect spinal cord damage in children and youth between birth and 21 years old at the time of injury.

Since then, funded by the NIH, the team has successfully employed an expanding array of imaging technologies to visualize in detail the original injury and subsequent pathologies. Those techniques have included the spinal cord cross-sectional area, which offers a structural biomarker for spinal cord atrophy and related pathology; and fiber tractography, which provides a 3D reconstruction of neural tracts using data collected by DTI.

Throughout the studies, the researchers have correlated biomarker-focused discoveries and observations of patients' clinical presentation. Now, they are ready to take the important next step: developing and testing projections for individual patients, based on comprehensive imaging studies of newly injured patients and multi-year tracking of their progress.

"To our knowledge, we are the only group seeking to define and validate pediatric SCI imaging biomarkers," Dr. Mulcahey observes. "We are excited about this work because it could fill a major gap in pediatric care—and, potentially, inform better treatment of adult SCI too." ■

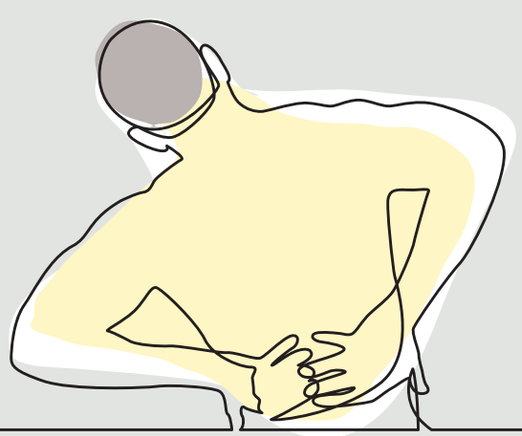
COUNTERING SPINAL DISC DEGENERATION

The pain caused by spinal disc degeneration affects millions of people worldwide and, too often, causes disability and opioid addiction. Current therapies for degenerative disc disease address only symptomatic relief. However, it may be possible to address the underlying problem by using endogenous stem cells to rebuild diseased or degenerated tissues.

Longtime research collaborators **Makarand Risbud, PhD**, James J. Maguire Professor of Orthopaedic Surgery, and **Irving Shapiro, PhD**, Gertrude and Anthony DePalma Professor of Orthopaedic Surgery, are working to understand the cellular mechanisms underlying disc degeneration, identify conditions that enhance disc cell survival and create tissue-engineering methods to regenerate healthy discs.

They are characterizing disc progenitor cells from both normal and diseased discs; then defining environmental conditions that enhance progenitor cell differentiation into cells that comprise the disc's inner tissue, the nucleus pulposus. Drs. Risbud and Shapiro hypothesized that adult mesenchymal stem cells (MSC) transplanted into the disc will assume nucleus pulposus-like characteristics and help restore degenerated disc tissue—and, thus far, they have shown that MSCs differentiate into nucleus pulposus-like cells under conditions similar to those existing in the disc in vivo.

On a parallel track, Drs. Risbud and Shapiro are characterizing a mouse model of spontaneous, early onset disc degeneration. (The lack of appropriate small-animal models has impeded research on the mechanisms underlying and driving the early onset process.) These models will also be important for testing the efficacy of the MSC-derived tissues. To date, the researchers have demonstrated that their mouse model recapitulates many features of human disc degeneration, including compromised cell survival and the changes to the cellular environment that lead to compromised tissue function. In addition, compared to control animals, the mouse model discs were stiffer, had decreased height and poor vertebral bone quality. ■



Architecture students designed a 3D model of Philadelphia in the year 2050 as part of Professor Edgar Stach's Highrise Buildings class on Smart Cities.

APPLIED//

BUILDING BETTER CITIES

CONTEMPORARY CITIES ARE, SIMULTANEOUSLY, ECONOMIC powerhouses and wells of extreme poverty; catalysts of efficiency and prodigious consumers of energy; places with excellent health care and unhealthy air. To a significant degree, the future of human society depends on our ability to resolve these contradictions by making cities "smarter"—i.e., healthier and more efficient, sustainable, economically productive and equitable."

Jefferson is applying its deep expertise in architecture, design, planning, material science and public health to a growing, multifaceted program of research on how to create (and recreate) cities as society needs them to be. Here are snapshots of how three faculty members are working toward that goal.

A Place for Addressing IDEAs

Kihong Ku, DDes, associate professor of architecture and Volpe Family Term Chair for Architectural Innovation, researches new technologies for addressing architectural design challenges, such as enhancing construction safety and developing new, sustainably created and energy-efficient building materials. He also works to improve the processes that underpin the conception and development of new products and solutions.

"There are tremendous opportunities for research and innovation in the building design process, and in how new construction materials are developed, and for meaningful cross-disciplinary collaboration in applying new technology to realize those opportunities," says Dr. Ku.

At Jefferson, architectural knowledge, expertise, creativity and advanced technical resources are fruitfully combined in the **Interdisciplinary Design and Experimental Architecture (IDEA) Studio**, which Dr. Ku founded and directs. The IDEA Studio is an innovative applied research framework for engaging and educating upper-level architecture students in cross-disciplinary design research that bears on open-ended questions.

In the IDEA Studio, faculty, outside practitioners and students from the fields of architecture, textile design, engineering, industrial design, medicine and others address various subjects. These include creation of novel 3D structures with textiles or textile-creation methods like knitting, and the use of such materials and methods to design and prototype adaptive building envelopes as a sustainable energy strategy. Underlying this approach is computational design thinking and technologies that enable teams of collaborators to analyze large amounts of data from multiple perspectives and to evaluate how building systems work, individually and in combination.

Studio participants learn from various sources, including computational and systems biologists who explore complex human biological processes through parametric and system modeling. The design of adaptive building envelopes can take advantage of similar approaches which adapt a material's intrinsic physical properties to create components and systems that react to environmental forces in a different manner.

"We can use evolutionary algorithms to simulate real performance and quickly run multiple iterations that model an array of scenarios to produce brilliant and unexpected solutions to architectural problems once thought intractable," notes Dr. Ku.

The future of human society depends on our ability to make cities "smarter."

Focusing on South Africa

For more than a decade, **Christopher Harnish, MArch**, associate professor of architecture, has focused his research and practice on resilient humanitarian architecture in South Africa which is the world's most quickly urbanizing area. Through the exploration and use of participatory design methodologies and high-performance/low-tech environmental strategies, Harnish has designed community, education and arts facilities in South Africa and Malawi. In addition, while serving as a Fulbright Teaching Scholar Fellow at the University of Malawi Polytechnic—where he guided Malawian architecture students in using design to advance equity, sustainability and resilience—he created a research-based design for the Malamulo Mission Hospital and its 80-acre hospital campus.

"Much of architectural research consists of high-performance, high-cost building assemblies—exceptional examples that serve narrow interests," says Harnish. "More important to me is exploring design processes and products that meet real needs of a broad swath of the population. This is especially important in the global South, where what is 'exceptional' is often impractical and unsustainable."

For that reason, Harnish is pursuing research projects that go well beyond traditional architecture and design topics—for example, collaborations on quantitative medical and public health research that will inform new healthcare facilities in South Africa. He is currently developing a collaborative research project in Malawi to improve the design of public health centers using evidence-based, quality-of-medical-care research. Those projects include analysis of facilities, needed to enable pregnant women to move closer to a distant hospital two weeks before their due dates, so that delivery care is immediately available; and spatial studies necessary to design hospitals that

enable small medical staffs and limited technical facilities to most efficiently and effectively serve a large number of patients.

The approaches that Harnish is bringing to architecture projects in the cities of South Africa have the potential to enhance the value and impact of community-focused architecture in regions throughout the world.

Concern for the Built Environment

Edgar Stach, Dipl.-Ing., professor of architecture, is a practicing architect and an internationally respected leader in research and design of smart cities, high-performance buildings and renewable energy technologies. His work focuses on energy efficiency, ecological sensitivity and responsibility, and reflects his concern for the built environment. He has received national and international design awards and recognition for his accomplishments in these areas.

Stach's current research centers on innovative techniques and advanced technologies for energy-efficient architecture. He serves as a joint faculty member at Oak Ridge National Laboratory's Building Technologies Research and Integration Center. Previously, he was a member of the faculty at University of Tennessee, where he founded multidisciplinary research platforms for high-performance buildings, sustainable architecture and solar energy harvesting. His ongoing focus on materials, technology and sustainability is supported through a mode of working that combines practice, teaching and research, as well as active engagement in the discourse of contemporary architecture through international design competitions and collaborations.

Stach has published more than 50 scientific papers and technical publications, and a scholarly book on architect Mies van der Rohe. He is currently writing a volume on Renzo Piano. The combination of knowledge, ideas, experience and skills that he brings to his research and his teaching are catalyzing today the conception and development of buildings that will comprise the cities of tomorrow. ■

Chris Harnish and biomedical engineering students from the Malawi University of Science and Technology captured drone footage that Jefferson students use to help redesign Malawi's Kamuzu Central Hospital.

APPLIED //

LANDSCAPE ARCHITECT as COMMUNITY TRANSFORMER

"ONE OF THE HALLMARKS OF CITIES WITH HIGH POVERTY RATES like Philadelphia is that children are profoundly disconnected from nature," notes **Kimberlee Douglas, MLandArch**, associate professor of landscape architecture and Anton Germishuizen Stantec Term Chair in Landscape Architecture. "My colleagues and I are investigating ways to recreate that connection and then observe the effects on health, community engagement and other key metrics."

Douglas believes that each landscape project must consider natural systems as well as social, historic and economic frameworks. This approach has driven her award-winning designs for projects such as the Cynwyd Heritage Trail—a rehabilitated brownfield rail corridor in Bala Cynwyd, PA—and the innovative, sustainable Linwood Avenue Neighborhood Park, in Ardmore, PA. It is also central to her applied research on ecological revitalization of urban neighborhoods and the benefits of nature for children in cities.

Developing "Green Networks"

Her current project is testing the development of "green networks," a series of small neighborhood nature parks that harness a hidden asset in many low-income neighborhoods—vacant lots. The project's ultimate objective is two-fold: enable every child to live within a 30-second walk of a green space; and create a verdant necklace running throughout the city's most economically depressed communities. Combining education and community engagement with research, Douglas employs local students to develop and use survey tools to observe and record characteristics of community strength and weakness and to photograph and map physical changes in the neighborhood.

Kimberlee Douglass, MLandArch, works with community members to set up small parks as part of a "green network" in Philadelphia.

"Philadelphia has roughly 40,000 parcels of open space," Douglas says. "They represent 40,000 chances to build safe green places, raise neighborhood property values and improve the health of children and adults alike." These parcels—and Douglas's initiative—also represent a model that can be adopted by cities across the country and around the globe.

Many of her colleagues agree: In 2019, Douglas earned the American Society of Landscape Architects' *Community Service Award*. "Her enduring and sustained community service has made a lasting impact on many neighborhoods in Philadelphia in providing quality green spaces in low-income neighborhoods," says **Barbara Klinkhammer, Dipl.-Ing.**, executive dean of the College of Architecture and the Built Environment. "She serves as an enthusiastic ambassador of the power of landscape architecture in transforming the urban environment." ■

BASIC// DISCOVERY

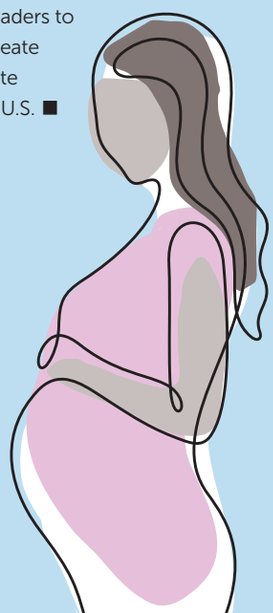
A CAREER ADVANCING MIDWIFERY

The year 2019 was a significant one—even for a clinician-researcher as accomplished as **Barbara Hackley, PhD, CNM**, associate professor of midwifery and women's health and the Dorothea Lang Term Chair. Prior to joining Jefferson in 2017 to launch and direct the Jefferson Doctor of Midwifery Program—the nation's first discipline-specific doctoral program for midwifery—Dr. Hackley served on the faculties of Georgetown, Columbia and Yale universities. And, during a career that has, thus far, spanned three decades, she received countless awards for her teaching and research—and for her clinical expertise in expanding mental health care, immunization, asthma care and obesity management services to pregnant and postpartum women.

Still, 2019 was special. Early in the year, Dr. Hackley and colleagues published the results of two important research studies. The first explored the impact of a community health center-based initiative to assist families in accessing New York City's pre-kindergarten program—finding that it resulted in substantially higher numbers of African American and Latinx families applying for and enrolling in the pre-K program. The second study, of group prenatal and well-baby care efforts, documented for the first time that those clinical interventions are associated with long-term benefits that persisted for two or more years. This study also revealed that perinatal group care was beneficial in areas not yet reported in the literature: nutrition, family communication and parenting.

Then, in May, Dr. Hackley was named a Fellow of the American College of Nurse-Midwives (ACNM) and was given the ACNM's *Lifetime Achievement Award* for service to the profession.

Topping everything off, the Jefferson Doctor of Midwifery Program graduated its first class and inaugurated a major national symposium, **Midwifery Thinks!**, which celebrates midwifery scholarship and innovation, and convenes midwifery leaders to share strategies and create coalitions to to promote maternal health in the U.S. ■



PURSUING the POTENTIAL for RNA BIOLOGY

RNA IS ESSENTIAL FOR THE PROCESS OF TURNING GENES' DNA instructions into the proteins that actually drive cellular functions. The field of RNA biology is dynamic and growing, as researchers discover the functions of a dizzying array of types of RNA. Jefferson's RNA biology program is multifaceted and rich with potential for both understanding human biology and developing ways to treat or prevent disease.

For example, **Ya-Ming Hou, PhD**, professor of biochemistry, guides a basic science research program addressing RNA's roles in a range of biomedical challenges, from cancer to antibiotic resistance. Recently, she may have identified an RNA-based vulnerability in gram-negative bacteria such as E.coli and Salmonella—which are antibiotic-resistant because their cells have two membranes and numerous toxin pumps that expel antibiotic molecules. Dr. Hou's group has shown that creating a defect in a specific transfer RNA (tRNA) undermines those defenses. This finding holds promise as a path for pursuing new, more effective antibiotics.

tRNA molecules are not a typical antibiotic target; they are part of the protein-building machinery cells need to function. But Dr. Hou's team found that to function properly, bacteria require the addition of a methyl group to one particular location on the spine of several tRNAs. When these tRNAs were deficient in methylation, the cells were more likely to have protein-building defects. Next, Hou's team created bacteria genetically deficient in tRNA methylation, and showed that the bacteria had more-permeable membranes and were less effective at pumping out chemicals, compared to normal bacteria. Finally, when the bacteria with defective tRNAs were exposed to antibiotics, they died faster and were less capable of developing drug resistance. The team is now screening molecules that could drive the same de-methylation effect as the genetic engineering; and, because the target in bacterial tRNAs is absent from human cells, the resulting drug could be less likely to have off-target effect on human cells.

Dr. Hou and colleague **Davide Trotti, PhD**, professor of neuroscience, have also been studying the role of specific tRNAs in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS)—pursuing investigations of a particular tRNA's role in the disease and whether it could be a therapeutic target. In that context, Drs. Trotti and Hou have undertaken an NIH-funded study on the most common cause of inherited ALS: a mutation resulting in patients having hundreds or even thousands copies of GGGGCC sequence in the gene C9orf72.

Ya-Ming Hou, PhD
Professor of Biochemistry

Davide Trotti, PhD
Professor of Neuroscience

Recent work by Dr. Trotti's group—in collaboration with **Aaron Haeusler, PhD**, assistant professor of neuroscience, and **Piera Pasinelli, PhD**, Frances and Joseph Weinberg Professor of Neuroscience and Director of the Jefferson Weinberg ALS Center—looked at what triggers these repeated sequences in the C9orf72 gene to eventually produce the toxic proteins associated with ALS (as well as with frontotemporal dementia and other neurodegenerative diseases in patients carrying the mutation). Suspecting that stressors may be a trigger, the investigators tested a number of agents that cause neurons to turn on the stress responses. Indeed, many of these also initiated production of toxic protein. The investigations also showed that neuronal over-excitation—similar to what happens during a seizure—also triggered the protein production.

Once the integrated stress response is activated, it is difficult to stop the production of the toxic proteins. But, by honing in on this over-arching cellular mechanism, the researchers gained insights on specific methods that might block the neuron-damaging response. The drug trazodone, which is approved for the treatment of depression, is known to act on parts of the integrated stress response. The researchers tested it in their repeat-mutation cellular model of the disease and found that it could block toxic protein-production. Now, they are screening for other molecules that might be even more effective at blocking the process. ■

COMPUTATIONAL MEDICINE CENTER UNCOVERS NEW RNA CATEGORIES

THE INTERDISCIPLINARY EXPERTS OF JEFFERSON'S COMPUTATIONAL Medicine Center combine high-performance computing, data-driven hypothesis generation and wet laboratory work to unravel the biology and role of short RNA molecules with powerful regulatory roles. The Center's research is led by **Isidore Rigoutsos, PhD**, Richard H. Hevner Professor of Computational Medicine; **Yohei Kirino**, associate professor of biochemistry and molecular biology; and **Eric Londin, PhD**, assistant professor of pathology, anatomy and cell biology.

The group has uncovered new RNA categories and many previously unsuspected molecules that act as regulators. They have also demonstrated that the identity and abundance of these newly discovered regulators depend on a person's sex, population origin and ethnicity—as well as on tissue type, tissue state and disease.

For example, the team has shown that the size and specific sequence of fragments of transfer RNA (tRNA) depend on the kind of cancer cell in which they are found: in their studies, the same parental tRNA produced fragments that differed depending on whether they were in, for example, breast cancer or prostate cancer cells. When the researchers analyzed broader data from a group of 32 cancers, they found an array of complex relationships among tRNA fragments, messenger RNA (mRNA), proteins, genomic architecture, repetitive elements and the mitochondrion. The work suggested that tRNA fragments are as important as the full-length parental molecules; that they have extensive interconnections to gene templates and gene products that differ by disease type; and that these interconnections can be affected by a person's sex. The findings could provide new angles of attack specific to the type of disease and the sex of the patient.

The investigators' analysis further revealed that all 32 cancer types harbor essentially the same tRNA fragments and mRNA, but in very different abundances. Moreover, the fragments and the mRNA associate with each other in specific pairs that differ in each cancer. Surprisingly, even though the tRNA fragments partner with different mRNA in each cancer, these mRNA belong to the same core biological processes. The discovery suggests more ways in which cancers might differ from one another—and suggests that expression of the same gene can go awry differently in different cancer types. "These tRF-mRNA associations could provide valuable insights for how to approach research into treatment," Rigoutsos notes, "because they capture different relationships in every cancer." ■

BASIC// DISCOVERY

Sunday Shoyele, PhD
Associate Professor of
Pharmaceutical Sciences

TREATING LUNG CANCER with NANOPARTICLES

NON-SMALL CELL LUNG CANCER (NSCLC)—THE MOST COMMON type of lung cancer—is very difficult to treat, but **Sunday Shoyele, PhD**, associate professor of pharmaceutical sciences, has developed a nanotechnology-based treatment. The new approach, which was effective in recent tests with mouse models, uses nanoparticles to deliver a molecule known to stall NSCLC tumor growth and believed to make cancer cells more susceptible to chemotherapy.

The molecule—microRNA 29b—is an example of the category of "silencing RNAs" (siRNAs) that interfere with the pathway by which individual genes are expressed. siRNAs are capable of both shutting down disease-causing processes in the cell and stripping away diseased cells' ability to resist treatments. The challenge is getting them intact to the point of disease. Dr. Shoyele's research program focuses on creating efficient and effective ways to deliver these therapeutic tools.

In the case of microRNA 29b, the problem is that the molecule quickly degrades in the bloodstream or is removed by immune cells. Therefore, Dr. Shoyele developed a special delivery mechanism. It is a nanoparticle comprised of three active parts: human immunoglobulin G, which cloaks the particle from the immune system; an antigen that seeks out lung tumors; and the therapeutic payload, microRNA-29b. Those three elements are bound together by a sticky polymer to form a spherical nanoparticle.

In the mouse models, the nanoparticles succeeded in reaching the tumors, which shrunk as a result. Dr. Shoyele is now pursuing comprehensive toxicity tests in animal models and is scaling up the nanoparticle manufacturing process—preparing for the treatment to enter clinical trials. ■

Dina Halegoua-DeMarzio, MD
Asssociate Professor of Medicine
Director of Jefferson Fatty Liver Center

CLINICAL // TRANSLATIONAL

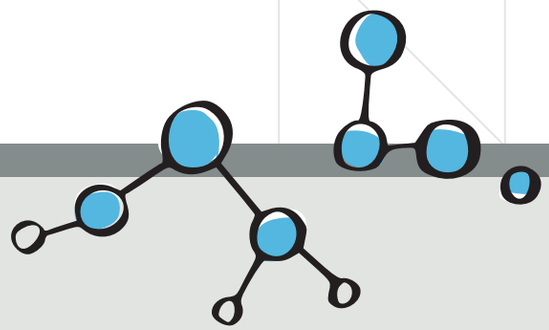
TREATING the MOST COMMON LIVER DISORDER

NON-ALCOHOLIC LIVER DISEASE, ALSO KNOWN AS FATTY LIVER Disease, is the most common liver disorder in western nations. Up to 30 percent of Americans have some level of the disease, and it will soon be the country's leading cause for liver transplant. As its name suggests, Fatty Liver Disease begins simply with storage of excess fat in the liver, but can progress into serious liver inflammation and to the extensive scarring of liver tissue known as cirrhosis.

Currently, biomedical researchers have a limited understanding of what causes the disease and drives its progression. **Dina Halegoua-DeMarzio, MD**, associate professor of medicine and director of **Jefferson's Fatty Liver Center**, and her colleagues are working to uncover the cellular mechanisms underlying the disease, in part by identifying associated conditions. "Although Fatty Liver patients are often overweight, suffer insulin resistance and diabetes, and have high cholesterol," Dr. Halegoua-DeMarzio explains, "we have found further associations with celiac disease and binge-eating disorders, and are investigating the exact relationships and cause-and-effect connections among these conditions."

There are no non-invasive methods of diagnosing the emerging condition. That is why the Fatty Liver Center is testing new diagnostic methods and conducting an array of clinical trials.

There is also much to be learned on the clinical level: There are no non-invasive methods of diagnosing the emerging condition—at present, liver biopsies are necessary—and no medications known to prevent or cure the disease. That is why the Fatty Liver Center is testing new diagnostic methods and conducting an array of clinical trials of potential therapies. Among the most promising drug studies are two phase III trials of treatments for patients with moderate liver scarring, and two phase II trials of therapies that show evidence of reducing liver fat levels and removing cholesterols that contribute to fat build-up in the liver. ■



BASIC // DISCOVERY

MODELING the SYSTEMS of LIFE

Rajanikanth Vadigepalli, PhD, professor of pathology, anatomy and cell biology, is a chemical engineer and systems biologist who views the body as a series of systems nested within systems, interacting in dynamic ways. He and his colleagues use high-powered computers to create complex models of how tissues and organs function, which they compare to observations of in vitro and in vivo lab models. The iterative process enables them to find minute, molecular level effects with outsized significance.

One of Dr. Vadigepalli's primary research focuses is the liver. He and his collaborators analyze the organ at molecular, cellular and tissue levels to learn how complex, cause-effect relationships trigger liver cells' normal regenerative activity (a surgically reduced liver usually regrows in months)—and, conversely, what happens when exposure to excess alcohol or fats overcome cells' regenerative capacity and the whole liver begins to fail. Their work is changing some long-held assumptions. For example, alcoholic liver failure has long been viewed as a process where the organ tolerates alcohol for a period and then suddenly decompensates at one catastrophic inflection point. However, Dr. Vadigepalli has found that alcoholic liver failure is actually a progressive process: damage accumulates over time as individual cells become more sensitive to injury with each passing insult; eventually, a tipping point is reached when too many individual cells lose function and the larger system—the liver—fails.

By helping to explain how systems actually work, Dr. Vadigepalli is opening new paths for diagnosing, treating and preventing an array of serious diseases and for bringing regenerative medicine ever closer to reality. ■

A DISTINGUISHED CAREER HONORED—

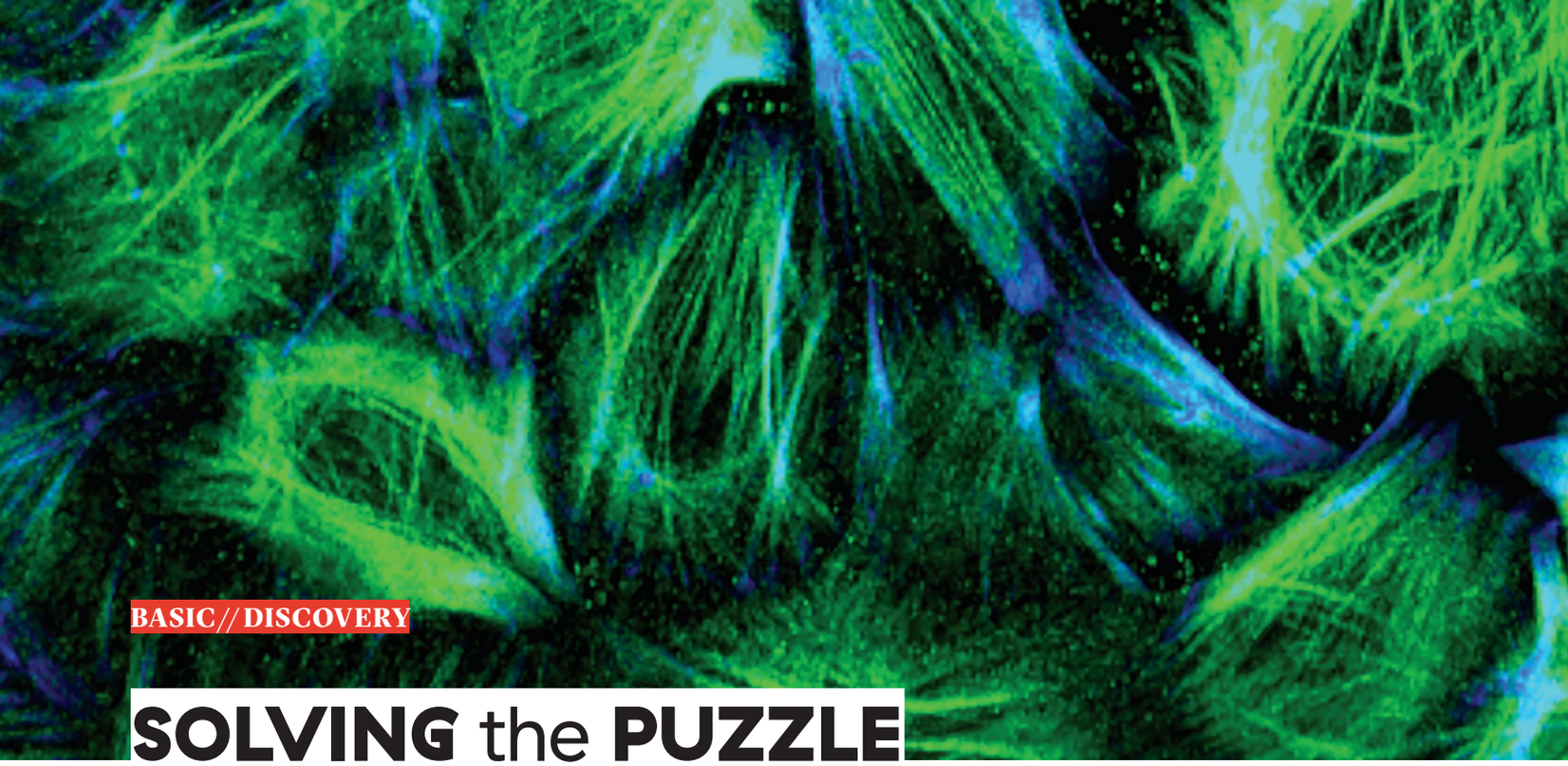
And the Work Continues

THE MOST PRESTIGIOUS AWARD IN INTERNATIONAL DERMATOLOGY—the World Congress of Dermatology's Alfred Marchionini Medal in Gold—is bestowed every four years, and in 2019, **Jouni Uitto, MD**, professor and chair of dermatology and cutaneous biology, was the humble recipient. The award is a recognition of Dr. Uitto's long and distinguished career, in which he has published nearly 900 peer-reviewed articles, textbook chapters and reviews—including 30 new publications over the past year.

Dr. Uitto is particularly renowned for his research on a group of genetic diseases called epidermolysis bullosa (EB), which manifest at birth with extensive skin blistering and scarring. In its most severe form, EB can be fatal during a child's first weeks or months of life. His lab discovered the disease's genetic basis: mutations in the collagen7A1 gene undercut the production of a protein necessary for keeping layers of the skin together. The lab then developed a transgenic mouse model of EB, which became a platform for development of treatment approaches. Today, five gene therapy approaches in clinical trial have their origins in Dr. Uitto's work.

He is also driving advances on the rare childhood disease pseudoxanthoma elasticum (PXE)—where mineral build-up in elastic fibers of the skin and blood vessels leads to formation of plaques in blood vessels and eyes that cause heart attacks and blindness. Collaborating closely with parents of children with PXE, Dr. Uitto gathered DNA samples that enabled his lab to identify the responsible genes. Today, clinicians can make a prognosis based on a patient's specific set of mutations, and research continues to develop and test effective therapies. ■

Jouni Uitto, PhD
Professor and Chair of Dermatology
and Cutaneous Biology



BASIC// DISCOVERY

SOLVING the PUZZLE of FIBROTIC DISEASES

UP TO 40 PERCENT OF DISEASE MORTALITY IN DEVELOPED countries results from fibrotic diseases, a family of conditions where the build-up of scar-like tissue interferes with the body's normal function. These conditions can be systemic (such as systemic sclerosis and scleroderma) or affect individual organs such as the lung, liver, kidney, heart or eye. Because the mechanisms underlying these conditions are poorly understood and treatments are few, Jefferson has made a major commitment to basic and translational research on a broad range of fibrotic diseases.

Pulmonary Fibrosis (PF) causes progressive, potentially fatal scarring of the lung. PF results, in part, from the inability of aging lung epithelial cells to regenerate after injury. This may be because aging cells do not direct nutrients to areas at greatest need after injury. **Ross Summer, MD**, professor of medicine, has been working to determine the interconnections between cellular metabolism and injury repair. His studies on young cells' metabolic adaptation to injury offer clues on how aging compromises the repair process—and suggests therapeutic approaches. For example, Dr. Summer has found that blocking lipid synthesis, alone, can cause fibrotic scarring in animal models; and, in counterpoint, has demonstrated that increased lipid production could reduce fibrosis-caused lung scarring significantly. He is now working to identify and test molecules that could have therapeutic effect by enhancing or protecting lipid synthesis.

Because scars that form in all injured tissues and organs are comprised primarily of collagen-rich fibrils, **Andrzej Fertala, PhD**, professor of orthopaedic surgery, has been developing an antibody to block an early step in fibril formation. Having shown the antibody to be effective at blocking fibril production in a mouse model of pulmonary fibrosis and a rabbit model of arthrofibrosis, Dr. Fertala is now fine-tuning it to create a therapeutic-grade biologic. Teaming with orthopaedic surgeons, Dr. Fertala's group is also testing the possibility of employing the anti-fibrotic antibody to block fibrosis of injured peripheral nerves, which hampers the nerve regeneration process.

Cataract surgery often results in a fibrotic disease known as Posterior Capsule Opacification (PCO), which can lead to loss of vision. **Sue Menko, PhD**, professor of pathology, anatomy and cell biology, developed a chick embryo model of PCO and uses it to identify cell-signaling pathways involved in fibrosis and to study other mechanisms of wound healing and fibrosis. These studies have led to a series of significant discoveries. For example, she and **Janice Walker, PhD**, assistant professor of pathology, anatomy and cell biology, found

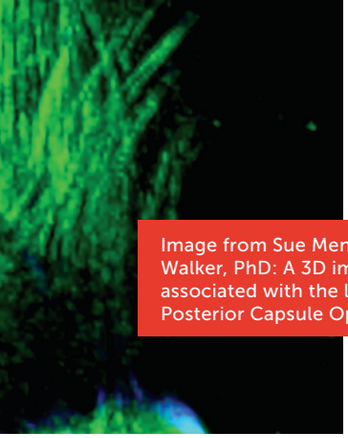


Image from Sue Menko, PhD, and Janice Walker, PhD: A 3D image of fibrotic cells associated with the lens fibrotic disease Posterior Capsule Opacification (PCO).

that the lens harbors a resident population of vimentin-rich mesenchymal cells that migrate to the wound edge, where they play a role in wound repair. Spurred by their encounter with a microenvironment of increased rigidly, these cells differentiate to myofibroblasts—the principal cell type associated with fibrosis. Subsequently, the researchers found that injury spurs the release of the protein vimentin, which binds to mesenchymal cells at the wound and helps signal the shift into a myofibroblast and the development of fibrosis. These findings may provide novel targets for development of new treatments for PCO.

Until very recently, the lens had been considered not susceptible to the immune processes normally associated with wound repair; most investigators assumed that immune cells played no role in PCO. However, using a lens-specific knockout mouse model, Dr. Menko's team found that degeneration of the lens activates an immune response both to the lens and throughout the eye (including cornea, vitreous humor and retina) that contributes to development of fibrosis associated with cataractogenesis. Additionally, they demonstrated that the lens is indirectly connected to the lymphatic system, providing a potential mechanism for the immune surveillance. Their findings have broad implications for understanding disease and injury-repair processes throughout the eye.

Children with a grave skin disorder known as butterfly disease (epidermolysis bullosa or EB) develop severe and chronic blisters and fibrosis within their connective tissues. The condition leads to club-like appendages where the skin grows over the fingers or toes. Andrew South, PhD, associate professor of dermatology and cutaneous biology, has shown that fibrosis also leads to an aggressive, often fatal, form of skin cancer in butterfly children. Recently, Dr. South and colleagues pinpointed how fibrosis develops in butterfly children—and demonstrated that a specific molecule interferes with the process and reduces fibrosis in a tissue-engineered model. Now his team is working to develop the molecule as a potential therapy for the debilitating condition. ■

THE JOAN & JOEL ROSENBLOOM CENTER for FIBROTIC DISEASES

Like cancer, fibrotic diseases are the result of complex biological processes that are similar in their final outcome, but diverse in the molecular mechanisms underlying those processes. Thus, identifying treatment targets and developing effective therapies is extremely difficult. It requires a continuous dialogue between basic scientists, translational researchers and clinical investigators across a range of disciplines.

The Joan & Joel Rosenbloom Center for Fibrotic Diseases, established in 2013, is an interdepartmental research program focusing on diagnosis, disease mechanisms, prevention and treatment of fibrotic diseases. It acts as a bridge: both to translate basic findings into drug therapies and to bring basic and clinical researchers together in novel studies that often cross fields and diseases.

Joel Rosenbloom, MD, PhD, professor of dermatology and cutaneous medicine, who directs the center, is a globally respected biomedical scientist. Now in his early 80s—with more than 50 years of research and nearly 400 peer-reviewed scientific publications under his belt—his active research program focuses on pulmonary fibrosis and abdominal adhesions.

He and his wife, Joan, founded the Center with a philanthropic gift soon after she was diagnosed with inoperable lung cancer in 2012. He credits several of his research breakthroughs to Joan, who worked as his lab manager for many years (after her pursuit of a PhD in physics was derailed by parenthood).

Today, he is frequently asked, "Why are you working so hard? Why aren't you retired?" Dr. Rosenbloom's response: "I think Joan would want me to be doing this. These are cruel, terrible diseases, about which we know too little to really help many patients. But by bringing smart researchers together from many parts of the institution—from cardiology, cancer biology, dermatology, nephrology, ophthalmology, pulmonology, radiation oncology and surgery—we are speeding progress in the search for common pathways that would allow us to finally understand and treat the full range of fibrotic diseases." ■

Jesse Roman, MD
Professor of Medicine

EXPLORING the EPIGENETICS of LUNG DISEASE

A recent study by **Jesse Roman, MD**, Ludwig Kind Professor of Medicine, found that a mother's diet can prompt changes in how her offspring's cells function. It offers clear and specific evidence that maternal experience can affect the health of following generations: in this case, that insufficient maternal nutrition during pregnancy can change the functioning of genes that affect lung health.

In the study, researchers examined lung-related genes in offspring of mice whose diet was limited during the second and third trimesters of gestation. They found that a handful of genes had a different level of expression in those progeny than did the genes in offspring of mice who ate normally. Two of those genes had particularly increased expression; both help keep intact the lining of blood vessels surrounding the lung's alveoli and promote their normal function. In addition, there was also increased expression of a gene that may predispose blood vessels to inflammation and clotting. Finally, the researchers also found higher levels of fibronectin—a connective tissue molecule that normally helps cells organize into tissues, but that sometimes attracts immune cells that prompt excessive inflammatory reactions, like asthma.

This research represents a **step forward** in understanding how follow-on generations' gene function can be affected by maternal or paternal experience.

Genetic mutations acquired by a mother during her lifetime are not themselves passed to subsequent generations. But changes in epigenetics—cellular activities driven by molecular processes not coded for in genes—can be passed from parent to child. This research represents a step forward in understanding how follow-on generations' gene function can be affected by maternal or paternal experience.

A next step for Dr. Roman and his colleagues is to explore in greater detail how altered gene expression affects lung function. It is possible that epigenetic changes in lung-specific genes—such as Dr. Roman found in his groundbreaking study—could be associated with the long-observed phenomenon of higher rates of lung disease in children born to undernourished mothers. ■

APPLIED //

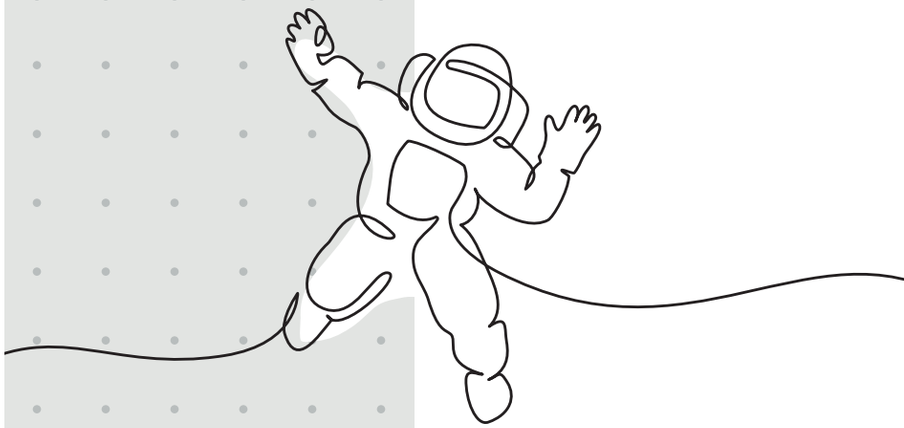
FUNCTIONAL FABRICS

From Mining Oceans to Walking in Space

THOMAS JEFFERSON UNIVERSITY TRACES ITS ANCESTRY, in part, to the 1884 founding of the Philadelphia Textile School, the nation's first center for textile-focused education. That institution continued to be a pioneer in textile science, technology and innovation for more than 130 years. Today, that legacy is visible in an array of nationally and globally recognized textile-related academic and research programs—notably including research, analysis and development of "functional fabrics" that serve a broadening range of purposes.

Jefferson is one of the few academic institutions possessing the full scope of expertise and technical facilities needed to reduce fundamental ideas to practice. As such, it fosters work ranging from discovery research and technical analysis of new materials, to design, prototype and development of formed products. Leveraging cross-disciplinary collaborations, faculty and students pursue basic science investigations; translate and apply their findings through ideation, prototyping and clinical or industrial testing; and develop production and supply-chain processes and marketing strategies. The resulting concepts, methods and products address the needs of a wide range of audiences, from healthcare providers and patients, industrial manufacturers and consumers, to United States government agencies and world-class athletes.

Jefferson has roots in the 1884 founding of the Philadelphia Textile School, the nation's first center for textile-focused education.



New Functional Fabrics and Garments

Since the 1970s, the University has produced high-performance material used to construct the gloves that NASA astronauts use during spacewalks. More recently, fashion design and engineering students developed creative outer-layer designs for the "Z-2 Prototype" of NASA's next-generation spacesuit. In 2017, a student team won top prize in a United States Department of Defense (DoD) challenge to redesign protective chemical-biological suits for U.S. warfighters. Their innovative concepts for materials and construction—a synthesis of original apparel design with the integration of new technologies—promised to significantly enhance comfort and improve tactility and dexterity during military action. The team has since worked with the DoD to bring their ideas and designs to reality.

Faculty and students have researched and developed new functional fabrics and garments for other kinds of high-intensity, high-stress situations. One is Olympic rowing, for which a team led by **Mark Sunderland, MS**, Robert J. Reichlin High-Performance Apparel Chair, created a seamless, single-piece uniform. Sunderland's group developed a new fabric and an innovative whole-garment knitting process, and created a uniform that fit like a virtual "second skin" for U.S. rowers in the 2016 Olympic games. He and his colleagues are now putting the finishing touches on new uniforms for the U.S. skeleton team preparing to compete in the 2022 winter games in Beijing.

New Medical Treatments

Continuing research and development of purpose-specific functional fabrics is also benefiting people with chronic disease or serious injury. Teams of clinicians, textile engineers and other technical experts are working at various stages of conceptualization, research and development of products. These include a functional vest for multiple sclerosis patients; fabric-based protective head garments for people with major head injury; polymer science-based fibers that hasten wound closure and healing; and a range of materials capable of sensing and transmitting clinically relevant biochemical or physiological changes. In the Edward P. Marram Biomedical Textile Structures Laboratory, researchers are pairing advanced textile structures with cultured stem cells to study the functionality of cell-covered textiles for medical use. One current project focuses on a potential 'cardiac patch' for treating coronary artery disease.

Novel Purposes

But functional fabrics have uses beyond garments and medical treatments. **Marcia Weiss, MFA**, associate professor of textile design, specializes in helping create new kinds of knitted and woven fabrics with novel purposes or unusual qualities—for example, fabric that conducts electricity in a way that causes it to change shape when subject to current. Weiss directs the state-of-the-art Fashion and Textiles Futures Center (FTFC), which focuses on textiles product design, engineering and function analysis, and enables student/faculty teams to partner with public and private organizations on innovative real-world projects.

"FTFC teams work on an extraordinary range of projects," explains Weiss. "We have designed fabrics that respond to heat and ice, and created novel products using completely new materials created by industry." For example, the Oak Ridge National Laboratories asked the team to help research and design a textile that would extract heavy metals from the sea, and they created a product that combined materials never before integrated together. "NASA engaged us to develop a fabric using carbon nanofibers, with layers as parallel as possible and linear strength running in one direction," says Weiss. "We created a very effective prototype, and they recently asked us to develop the next phase of the fabric."

Brian George, PhD, associate professor of engineering, is a textile engineer and materials maker whose primary research focuses on converting non-traditional materials into nonwoven fabrics for a variety of uses. He and colleagues, **Diana R. Cundell, PhD**, professor of biology, and **Alexander Messinger, MSArch, MArch, MCP**, professor emeritus, have developed new biocidal textiles that naturally kill bacteria, mold and fungi. Such materials have many potential uses, including kitchen countertops and "breathing wall" systems capable of killing bacteria in hospital rooms and physicians' offices. On a different track, Dr. George is investigating uses of waste fibers from manufacturing hats and other felt-based products. His purpose here is to explore the fibers' potential for increasing the strength of concrete and other building composites and for enhancing soil fertility for agriculture. ■

APPLIED //

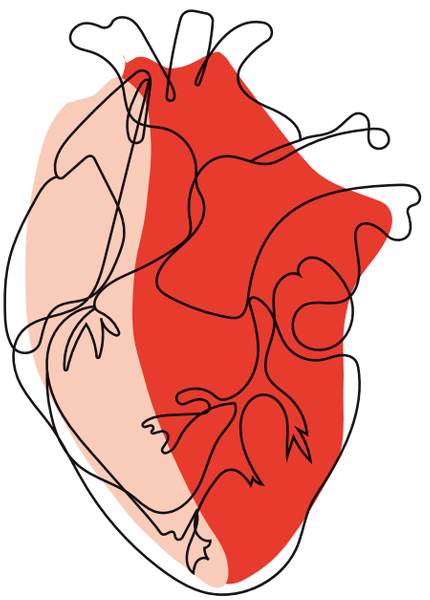
NEW SPACE and NEW NAME for MATERIALS TESTING LAB

Jefferson's technical facilities for research, development and testing of new fabrics may be unsurpassed in higher education: **Grundy Materials Evaluation Laboratory** has been assessing new and newly combined materials for more than 40 years. This year, it will have a new name and a new home. Thanks to the support of noted textile design alumnus Jeff Bruner '73, the **Jeff Bruner Materials Characterization Laboratory** will open in the state-of-the-art Kay and Harold Ronson Health and Applied Science Center this spring.

The Lab's main mission remains the same: to offer experiential learning, introducing students to technology and processes for evaluating materials. It has also been a problem-solving workhorse for industry and government agencies, with the capacity to assess myriad factors, including friction, wicking, strength, weight, high-compression capacity and abrasion/snagging resistance.

"One of our more complex studies was the seven-years-long War Fighters' Apparel project," explains Janet Brady, MS, associate professor of materials technology and the Lab's faculty director. "To perform full functional testing of potential military garments—notably, to evaluate comfort and material strength and durability—we formed multidisciplinary teams, including computational analysts, computational chemists, psychologists and human-factor specialists, textile engineers and garment-development experts. DoD adopted many of the garment-design details that we recommended." ■

REDUCING IMPLANTABLE DEVICE INFECTIONS



EVEN AS JEFFERSON RESEARCHERS HELP ADVANCE MEDICAL care by developing wholly new treatments, methods and tools, they are also working hard to reduce complications associated with procedures performed by tertiary care centers across the country. Post-procedure infections, in particular, can be a pernicious and costly problem. Clinician-scientists throughout the Jefferson system are pursuing clinical trials that aim to address the problem.

For example, **Arnold J. Greenspon, MD**, professor of medicine and director of the **Jefferson Cardiac Electrophysiology Laboratory**, is working to address the problem of infections associated with cardiac implantable electronic devices (CIEDs), such as pacemakers, implantable cardioverter-defibrillators and cardiac resynchronization therapy devices. While any medical device or product implanted in the human body can become infected, hospitals across the country have seen the rate of CIED infection grow faster than that of other types of device implantations. These patients must return to the hospital to have the device removed and to undergo antibiotic treatment. Subsequently, they must have a replacement implanted.

Surgical site infections can be devastating to patients; consequences can include sepsis, limb loss and even death. In addition, these infections can be costly to our nation's healthcare system, adding an average of 4.3 days to hospital stays and $10,497 per patient to the overall cost.

"Although overall infection rates are very low—currently, only about one percent of recipients develop a CIED-related infection—they are bad experiences for patients, potentially even fatal," says Dr. Greenspon.

Moreover, a study he co-authored last year found that CIED infections are quite costly—with expenditures for Medicare fee-for-service beneficiaries ranging from $22,000 to $77,000 per case.

Studies to Prevent CIED Infections

For those reasons, Dr. Greenspon has been collaborating in a series of research studies seeking to define the factors that cause these infections to develop. He has also partnered in an array of multi-center trial approaches for reducing the rate of CIED infection. A report on the most recent of those trials, centering on an absorbable, antibiotic-eluting mesh "envelope" for the CIED, was published recently in New England Journal of Medicine. It showed that use of the antibacterial envelope resulted in a significantly lower incidence of major CIED infections than standard-of-care infection-prevention strategies alone, without notable added complications.

Now, Dr. Greenspon is collaborating with researchers at Vanderbilt University on a trial with

patients at high-risk for CIED infection. It will seek to determine if use of the antibacterial envelope with an additional, post-procedure application of systemic antibiotics will further reduce incidence of infection.

Reducing Infections in Vascular Procedures

Paul DiMuzio, MD, MBA, William M. Measey Professor of Surgery and director of **Jefferson's Division of Vascular and Endovascular Surgery**, has led two studies on the use of a "negative pressure therapy" to reduce infections at the incision site in vascular surgical procedures. Both studies compare standard surgical dressings with the PREVENA™ Dressing Kit, a negative pressure dressing that continuously drains exudates from surgical incisions, which is applied immediately in the operating room.

The first study, published last year in the *Journal of Vascular Surgery*, focused on vascular groin incisions, where complications rates are as high as 44 percent, nationally. The randomized controlled trial focused on 119 femoral artery incisions considered high-risk for complications. Compared to patients receiving standard dressing, the negative pressure therapy resulted in significantly fewer wound infections (9 percent), reduced patient reoperation and readmission and an average savings of $6,045 per patient.

The second study, now in progress, is testing negative pressure therapy for surgical wounds following lower-leg amputation. Wound complications in this setting have been reported as high as 34 percent nationwide. This multi-center trial aims to enroll 440 patients who will undergo above- or below-knee amputations at one of six participating medical centers in the United States and Europe. Results from the study are expected to be available in late 2021.

"We are particularly excited about the potential for reducing wound infections for this patient population, many of whom are suffering from peripheral vascular disease, diabetes or heart failure and are particularly vulnerable to post-surgical infections," says Dr. DiMuzio. ■

CLINICAL// TRANSLATIONAL

SIGNS of HUMANITY

People who use signs to ask for help ("panhandle") are a very visible fraction of a city's underserved or homeless population. Yet, they are rarely heard. The signs they carry are artifacts of this phenomena, but they do not tell the complete story.

The Signs of Humanity Project was a researcher-artist collaboration that explored the interactions between people who are "panhandling" and those who pass by.

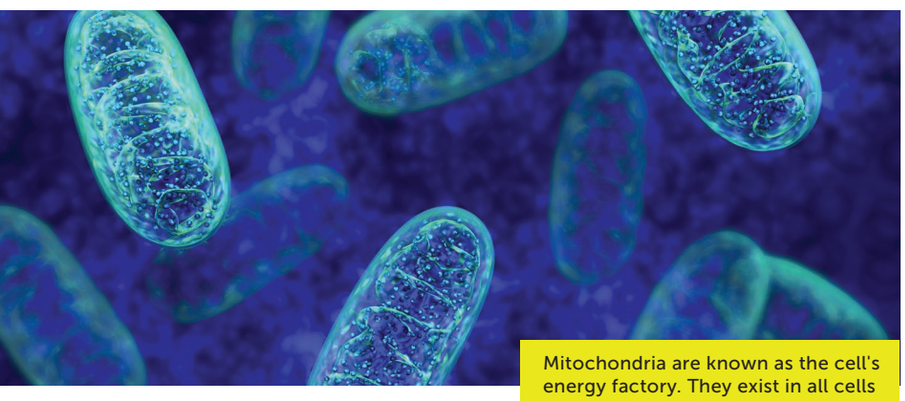
The Project's research arm qualitatively explored the experiences of people who panhandle; and its artistic arm created an exhibit intended to mitigate this community's dehumanization. In July 2018, artist **Willie Baronet** worked with **Rosie Frasso, PhD, CPH**, public health program director, and a team of MPH and MD students to begin data collection and artifact acquisition. Baronet purchased more than 100 signs from their owners—paying on average $10 for each and offering materials with which to make a new sign. Those who sold their signs were then asked to participate in a brief interview where open-ended questions explored their interactions with passersby, their opinions about how money collected is used by other people who panhandle and their perceptions of how the opioid crisis has affected them.

In September 2018, Baronet curated an exhibit of the signs purchased on the streets of Philadelphia. In addition, during a special public program at the exhibit, Dr. Frasso and the student team presented their preliminary research findings. Key among those findings was the fact that the great majority of interview respondents reported feeling invisible and isolated, and noted that the opioid crisis exacerbated their sense of isolation. On the other hand, they reported feeling both comfortable and pleased that their signs would be used in an exhibit designed to get people talking about homelessness.

Baronet also gained a novel perspective from the project—that of a researcher. He observed that, "It was cool to be working with students who are so analytical and research driven and had a huge level of compassion and empathy." ■

POWERING RESEARCH on MITOCHONDRIAL DISEASE

MITOCHONDRIA ARE SPECIALIZED STRUCTURES THAT EXIST in all cells except red blood cells. Generally known as the cell's energy factory, mitochondria play a much broader role: from helping in the processes of making hemoglobin, detoxifying ammonia in the liver, metabolizing cholesterol and neurotransmitters and synthesizing estrogen and testosterone. Each year, thousands of children (and, increasingly, adults) are diagnosed with genetic mitochondrial conditions that range from skeletal muscle weakness and exercise intolerance to neurodegenerative diseases, heart disease and liver failure. In addition, mitochondria are increasingly recognized as playing a role in the pathology of diseases such as diabetes and cancer.



Mitochondria are known as the cell's energy factory. They exist in all cells except red blood cells.

Jefferson's Center for Mitochondrial Imaging Research and Diagnostics—known as the MitoCare Center—investigates mitochondrial energetics, signaling and dynamics to learn how changes in mitochondrial biology cause disease and to identify potential targets for new treatments. Fundamental to MitoCare Center researchers' work is advanced microscopy that—combined with cutting-edge metabolic technologies, genetics and proteomics—enables them to observe mitochondria functioning in both normal and diseased tissues. These capacities also enable Center investigators to create better methods of diagnosing mitochondrial diseases and testing potential therapies.

MitoCare comprises five core research teams, plus an array of associated multidisciplinary teams whose research crosses into mitochondrial biology. The team led by MitoCare director **Gyorgy Hajnoczky, MD, PhD**, the Raphael Rubin, MD, Professor of Pathology, Anatomy and Cell Biology, was among the first to visualize mitochondrial energy metabolism and ion transport in single live cells. This work helped to elucidate fundamental signaling mechanisms that coordinate mitochondrial action with broader cellular function. His team has also been developing live cell imaging capacity that allows bioscientists from many disciplines to study intracellular processes.

MitoCare researchers are also applying the Center's technical capacities to study mitochondria's precise role in specific diseases. For example, **Erin Seifert, PhD**, associate professor of pathology, anatomy and cell biology, is pursuing two NIH-funded studies on the multifaceted role skeletal-muscle cell mitochondria play in the development of disease—including an investigation of how malfunctioning muscle mitochondria can undermine glucose regulation throughout the body, leading to type 2 diabetes. **Shey-Shing Sheu, PhD**, professor of medicine, and **Gyorgy Csordas, MD**, associate professor of pathology, anatomy and cell biology, are working to define the central role that mitochondria play in the development of ischemic heart disease, cardiac arrhythmias, cardiomyopathy and heart failure. And **Dmitry Temiakov, PhD**, associate professor of biochemistry and molecular biology, studies how the process of DNA transcription and replication in mitochondria differs in normal versus cancer cells. ■

ABOUT THOMAS JEFFERSON UNIVERSITY

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

8,100+ students

65,000+ alumni

$954,000,000+ endowment

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

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

- COLLEGE of ARCHITECTURE & THE BUILT ENVIRONMENT
- COLLEGE of HEALTH PROFESSIONS
- COLLEGE of HUMANITIES & SCIENCES
- COLLEGE of LIFE SCIENCES
  - —GRADUATE SCHOOL of BIOMEDICAL SCIENCES
- COLLEGE of NURSING
- COLLEGE of PHARMACY
- COLLEGE of POPULATION HEALTH
- COLLEGE of REHABILITATION SCIENCES
- KANBAR COLLEGE of DESIGN, ENGINEERING and COMMERCE
  - —SCHOOL of BUSINESS
  - —SCHOOL of DESIGN and ENGINEERING
- SIDNEY KIMMEL MEDICAL COLLEGE
- SCHOOL of CONTINUING and PROFESSIONAL STUDIES

RESEARCH FUNDED IN 2019

378 externally funded Principal Investigators

967 active grants

$153,985,074 in grants—from funding organizations ranging from the National Institutes of Health (NIH), the US Department of Defense and the Pennsylvania Department of Health to the Nancy Laurie Marks Foundation to the Genentech, Merck and Celgene corporations

$79,303,921 in NIH funding in 2019—a 31% increase since 2015

CLINICAL RESEARCH AS OF JANUARY 2020

1,062 active studies across **33** departments

245 clinical research personnel

340 funded Principal Investigators

LOOKING AHEAD: NEW BIOMEDICAL RESEARCH BUILDING PLANNED for CENTER CITY CAMPUS

Thomas Jefferson University received a $70 million gift from Sidney and Caroline Kimmel to advance research at the University. The gift will support the new **Caroline Kimmel Biomedical Research Building**, which will be a home for big ideas and will provide Jefferson scientists with leading-edge technology and laboratories. The new facility will markedly expand Jefferson's research capacity and create a "research corridor" that facilitates connections and collaborations among researchers across the University. ■

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BASIC/DISCOVERY
CLINICAL/TRANSLATIONAL
APPLIED

Academic Areas of Interest

ARCHITECTURE
BUSINESS
DESIGN
ENGINEERING
FASHION & TEXTILES
HEALTH
MEDICINE
SCIENCE
SOCIAL SCIENCE

Advancing and applying knowledge to **improve lives.**

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