FALL 2018

BIOMEDICAL ENGINEERING

UNIVERSITY OF WISCONSIN-MADISON

GLOBETROTTERS:

MAJOR AWARDS PROPEL BME GRADUATES

CHAIR'S MESSAGE

Greetings!

The UW-Madison campus is buzzing with activity for another academic year. It's a busy—but exciting—time in the Department of Biomedical Engineering.

The summer of 2018 included two major developments that will create new possibilities for our faculty and students.

In early September, UW-Madison, the state of Wisconsin and biohealth industry leaders launched the Forward BIO Initiative, a public-private partnership that will bolster biomanufacturing discovery and entrepreneurship in our state. As part of the effort, our own Bill Murphy, the Harvey D. Spangler Professor, will lead the new Forward BIO Institute on campus. I can't think of anyone better suited for the role than Bill, who's created several successful biomanufacturing companies and brings a unique combination of academic and industry knowledge.

A few weeks earlier, the university announced a $100 million partnership with Foxconn Technology Group that will fund a new interdisciplinary research facility on our engineering campus. It will also create new research opportunities in areas such as genomics, immune cells, clinical data integrity and processing, and medical imaging in cancer and related diseases.

Yet those aren't the only reasons for excitement in BME.

Our newest faculty member, Associate Professor Kip Ludwig, is an expert in using minimally invasive techniques to manipulate the nervous system and treat disease. He's also one of my longtime research collaborators, so I know firsthand how fortunate we were to hire him. We also have three more new faculty members starting in January: Aviad Hai, Melissa Kinney and Colleen Witzenburg.

And, as always, our students continue to impress. In this newsletter, you can read about two 2018 graduates who are pursuing ambitious work in India as Fulbright Scholars, plus two sophomores who used a first-year design project to help women in rural Kenya.

Visit our website (www.engr.wisc.edu/bme) throughout the year to read about the latest BME news, and be sure to connect with us on Facebook (@UWBME) and Twitter (@UWMadison_BME).

ON, WISCONSIN!

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Productive partnership

UW-Madison Chancellor Rebecca Blank (center) and College of Engineering Dean Ian Robertson (second from right) give Foxconn Technology Group representatives, including Chairman Terry Gou (right), a tour of the engineering campus in August 2018. Foxconn's $100 million investment in UW-Madison includes funding to help establish a new interdisciplinary research facility for the College of Engineering. *Photo: Bryce Richter.*

MORE: **www.engr.wisc.edu/100-million-foxconn-gift-launches-major-new-partnership-uw-madison/**

FOCUS ON NEW FACULTY

LUDWIG HIJACKS THE NERVOUS SYSTEM

Instead of taking a daily pill, a patient relies on a tiny implanted electrode to stimulate a nerve and cue delivery of biomolecules already produced by the body. The drug arrives right when and where it's needed and in the precise quantity the patient needs.

That's part of Associate Professor Kip Ludwig's vision for the future of medicine. Ludwig works in the world of neural engineering—"hijacking" the nervous system, as he puts it—with a particular focus on small, injectable devices. To him, they represent the next generation of therapies within the realm of neuromodulation, which broadly refers to stimulating nerves to treat disease.

"It's the ultimate in personalized and precision medicine," says Ludwig, who's also the neuroengineering lead at the Grainger Institute for Engineering. "Precision because we can deliver a drug exactly when we want, where we want, how we want, but personalized because these things are smart and have sensors and they can sense and maintain your exact levels throughout the day."

Ludwig joined the university in summer 2018 and brings a unique blend of academic, industry and federal agency experience.

He's spent the past three years as associate director of Mayo Neural Engineering Laboratories at Mayo Clinic in Rochester, Minnesota. Before that, he directed the neural engineering programs at the National Institutes of Health (NIH), where he also led the majority of NIH device programs tied to the White House BRAIN Initiative and created a program to fund research aimed at better understanding the nervous system's relationship with organs.

Ludwig also worked as a senior research scientist at CVRx, a Minnesota-based medical device startup. There, he designed CVRx's next-generation device, the BAROSTIM NEO, an implanted electrode that slows down the heart and dilates blood vessels to relieve hypertension in patients who have been diagnosed with heart failure.

Ludwig is a longtime collaborator with Vilas Distinguished Professor and department chair Justin Williams. The two are co-principal investigators on a nearly $10 million, six-institution grant from the U.S. Defense Advanced Research Projects Agency (DARPA) to use electrodes to stimulate nerves in the head and neck and put patients into an optimal learning state.

Ludwig and Williams are also exploring potential applications for neuromodulation in treating neurodegenerative diseases.

MORE: **www.engr.wisc.edu/focus-new-faculty-ludwig-hijacks-nervous-system/**

BIOMANUFACTURING MOVES FORWARD IN WISCONSIN

William Murphy, the Harvey D. Spangler Professor, will help lead a new collaborative effort to make Wisconsin a recognized center of excellence for biomanufacturing.

The Forward BIO Initiative will offer resources to efficiently translate innovations into commercial products in biomanufacturing. The initiative comprises the Forward BIO Institute, based at UW-Madison; Forward BIOLABS, a nonprofit shared laboratory facility housed at University Research Park on Madison's west side; and BioForward Wisconsin, which will facilitate partnerships between government, academia and private industry.

"The Forward BIO Initiative will have everything it takes to amplify the impact of Wisconsin's innovations in biomanufacturing," says Murphy, who is chair of the initiative and director of the Forward BIO Institute.

The Forward BIO Institute will catalyze innovation in biomanufacturing research, entrepreneurship and workforce development, and act as a "catapult" that pushes groundbreaking technologies into the private sector.

The institute will establish a new master's degree program in biomanufacturing innovation.

"We are a technology development and training entity," Murphy says. "We want to not just develop next-generation technologies, but to train the next generation of students that can lead technology development in industry."

A $750,000 grant from the Wisconsin Economic Development Corporation established the initiative, while the Wisconsin Alumni Research Foundation has provided $200,000 of seed funding for Forward BIOLABS.

The College of Engineering, the Grainger Institute for Engineering, the School of Veterinary Medicine and the School of Medicine and Public Health will provide support for the institute, including space and funds for technology development and three new faculty hires in advanced biomanufacturing.

FULBRIGHT FRIENDS BREAK ENGINEERING MOLD

To understand why Kayla Huemer and Hannah Lider are such close friends, you need to look to the country in which the two recent UW-Madison biomedical engineering graduates are living and working as 2018-19 Fulbright Scholars.

In India, there's a term—jugaad—that cuts across a few of the country's 22 officially recognized languages and is essentially equivalent to a "MacGyvered" solution: creating an innovative fix despite a lack of resources.

"There's a certain pride in the spirit of jugaad that makes it fundamental to understanding Indian culture," Huemer says.

"It's such a staple in the way both of us think," adds Lider, who's spent two previous summers in India and has become an advanced speaker of Hindi, the most prevalent language in the country. "Sometimes you've just got to make it work the best you can with what you have."

It's this type of innovative mentality that helped the pair flourish in the BME program, and it is no doubt serving them well as they take up their Fulbright research projects on opposite ends of India.

While more than 1,900 students from around the United States, including 19 from UW-Madison, are participating in the prestigious Fulbright U.S. Student Program during the 2018-19 academic year, Huemer and Lider are relative rarities as Badger engineers.

There have only been six previous College of Engineering graduates who have earned spots in the Department of State-sponsored program, which dates to 1946 and funds study, research or English teaching in foreign countries for an academic year.

Huemer and Lider's friendship started in the BME undergraduate design curriculum. After Lider participated in the S.N. Bose Scholars Program, which sends American students to India to work in research labs for a summer, she encouraged her friend to apply.

Kayla Huemer

Hannah Lider

Huemer did, and while working at the Indian Institute of Science in Bengaluru, she uncovered the project she'll continue to work on through her Fulbright grant: a wearable device to measure pressure points in the feet of diabetic patients.

"Ever since I was little, I wanted to be a doctor who works in the jungles of the Amazon," says Huemer, whose father came to Madison from Austria on a Fulbright, met her mother and settled in the United States. "I was always interested in medicine, but until I came to UW-Madison, I didn't know what an engineer was. And now, I feel so fortunate that Fulbright will allow me to combine my interest in low-resource healthcare with the biomedical engineering skills I've developed at UW-Madison."

Lider is also revisiting an old connection in India. While studying Hindi on a Critical Language Scholarship in 2016, she visited Barefoot College, an organization that spreads self-sufficiency and sustainability to impoverished rural communities.

After spending three months further studying Hindi through a Fulbright Critical Language Enhancement Award, she'll split her time between two projects with Barefoot's traveling women's health clinic: one devising a more accurate and efficient test for measuring hemoglobin to screen for anemia in pregnant women; the other helping to digitize the clinic's records, which cover 40 villages.

MORE: **www.engr.wisc.edu/fulbright-friends-break-engineering-mold/**

As a senior, Kayla Huemer received the Ferraro Family Scholarship, an award open to BME undergraduates. With the financial support, she was able to devote more of her time outside of class to her design projects, her work in independent research and her passion as a trombone player in the UW Marching Band for all five years of her undergraduate career.

METASTASIS FINDINGS COULD UNLOCK NEW OVARIAN CANCER TREATMENTS

In order to spread their destruction, ovarian cancer cells must break free from their tumor home, travel through the fluid in the peritoneal cavity, and attach to the outside of the abdominal organs—surfaces that are, by necessity, not sticky.

Despite these challenges, most patients with ovarian cancer are diagnosed after metastasis has begun, resulting in poor patient outcomes. While ovarian cancer is only the 11th-most common form of cancer among women in the United States, it accounts for the fifth-most deaths, according to the Ovarian Cancer Research Fund Alliance.

New research from the lab of Associate Professor Pamela Kreeger has identified one way ovarian cancer cells appear to successfully spread. The work, detailed in a paper published in *Cancer Research*, could lead to new therapies to curb metastasis of these tumors.

"Like most cancers, it's not the primary tumor that's usually the problem. It's the spread of the tumor to nearby organs that leads to serious complications," Kreeger says. "So if you can slow that process down, it's possible the patient will live longer and/or have a better quality of life."

In studying high-grade serous ovarian cancer, the most common but also most aggressive type, Kreeger, postdoctoral fellow Molly Carroll (PhD '17) and other lab members have teased out how one type of immune cells helps cancer cells attach in the peritoneal cavity, enabling metastasis. Higher levels of these immune cells, called alternatively activated macrophages, are associated with worse outcomes.

But the question remained: Do these macrophages encourage metastasis? Experiments revealed macrophages increase tumor cell attachment to the mesothelial cells—by making the mesothelial cells stickier.

"For me that was one of those scientific 'ah ha' moments—the interactions between the normal cells in our body can influence metastasis. In other words, it's not *all* about the tumor cell," says Kreeger.

Computational modeling revealed the proteins responsible: The macrophages produce a protein called MIP-1β, which causes the mesothelial cells to produce more of an adhesion protein called P-selectin. That, in turn, allows the cancer cells to stick.

The good news: There are already several existing drugs, developed for other diseases, that could prove useful. Maraviroc, which is used to treat HIV, inhibits the receptor for MIP-1β, while two different drugs that target P-selectin are in clinical trials for blood disorders.

"We're interested in pursuing multiple avenues, because it's possible one will work better than another," says Kreeger. "It's also possible one will have more tolerable side effects than another."

MORE: **www.engr.wisc.edu/metastasis-enablers-findings-unlock-new-ovarian-cancer-treatments/**

NIH award helps McClean decode cellular responses

When a stimulus descends upon a cell, it sets off a flurry of activity. Sensors on the surface take in information and relay it inside to other proteins, which perform computations and transmit their findings. The cell makes a decision and responds to the stimulus.

Assistant Professor Megan McClean wants to figure out how it all works—and then manipulate the process.

"How can I predict what a cell's going to do and how can I make it do exactly what I want it to do? I find that really interesting. It's the secret control freak in me," she jokes.

McClean studies cellular signaling pathways, the biological networks that transform external signals into internal decisions such as whether to grow or die. It's fundamental work with implications for identifying drug targets and designing medical treatments.

Her work to better understand and engineer those signaling processes will get a boost, thanks to a Maximizing Investigators' Research Award from the National Institutes of Health that provides her with $1.8 million over five years. In addition to supporting the range of research projects in her lab, it affords her the flexibility to pursue new questions as they emerge.

"We can grow and pivot and change direction as new things come up, which is really great, because a lot of science happens unexpectedly," she says.

MORE: **www.engr.wisc.edu/reading-signals-nih-award-helps-mcclean-decode-cellular-responses/**

Uncovering hidden drivers of ovarian cancer

Associate Professor Pam Kreeger, Vilas Distinguished Professor Kristyn Masters and Professor Paul Campagnola are using a five-year, $2.2 million grant from the National Institutes of Health to study changes in the extracellular matrix that drive ovarian cancer progression and create representative in vitro models.

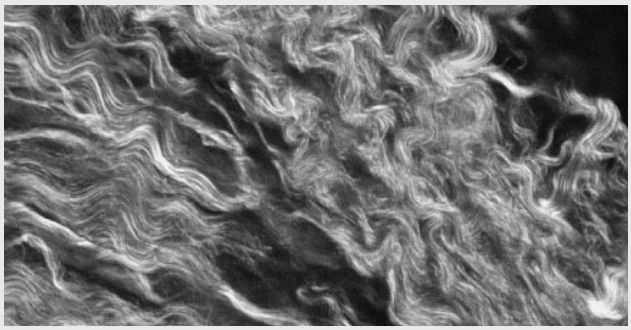
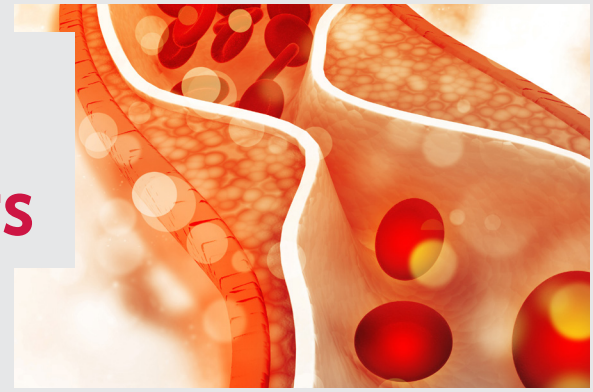


Image: Paul Campagnola.

An image of collagen fibers in cancerous tissue.

A STENT-FREE FUTURE FOR COMMON CARDIOVASCULAR AILMENTS



When a patient is suffering from a clogged artery, there's a go-to procedure: performing an angioplasty to open up the vessel and placing a tube, called a stent, inside to keep it open. Modern stents even offer the ability to release drugs to prevent future closures.

But there are downsides to these drug-eluting stents. While the medication stops the overgrowth of smooth muscle cells that cause re-narrowing—a process called neointimal hyperplasia—it also poisons the endothelial cells that form the inner wall of the blood vessel. And the presence of a physical object increases the risk of blood clots.

Vilas Distinguished Professor Shaoqin "Sarah" Gong and her collaborators, Dr. K. Craig Kent and Professor Lian-Wang Guo of The Ohio State University College of Medicine, believe they've found a better strategy for maintaining open blood vessels in the wake of surgeries such as angioplasties or bypasses.

The collaborative team received a $2.4 million grant from the National Institutes of Health to develop a new, stent-free approach using nanoparticles to deliver a drug.

The four-year grant builds upon promising preliminary studies in which the Ohio State researchers identified potential drug targets and Gong, an expert in nanomedicine, devised a delivery method by engineering biomimetic nanoclusters to carry a drug to the appropriate location. The group details that preliminary work in a paper published in the September 2018 issue of *Biomaterials*.

By inhibiting the targeted pathways, the researchers believe they can suppress smooth muscle cell proliferation while also protecting the endothelial cells and allowing them to re-grow after surgery. To safely deliver a drug to do that, they'll rely on Gong's drug-loaded nanoclusters, which are coated with a biomembrane, such as a platelet.

After doctors inject the nanoparticle through an IV, its biomembrane coating would act as a guide to take the particle to the targeted location, says Gong.

"You want to deliver your drug more specifically to the injured vasculature," she says.

MORE: **www.engr.wisc.edu/stent-free-future-common-cardiovascular-ailments/**

INFLAMMATORY WORK: BEEBE TAKES A CLOSER LOOK AT SCIENCE BEHIND SWELLING

In the coming decades, David Beebe expects the public to become more and more aware of the links between chronic inflammation and a whole host of ailments.

"It's likely implicated in almost every disease," says the John D. MacArthur Professor and Claude Bernard Professor, rattling off a list of illnesses that includes cancer, cardiovascular conditions and autoimmune diseases. "But it's been really difficult to study and we don't know a lot about it."

Beebe and longtime collaborator Anna Huttenlocher, a professor of medical microbiology and immunology and pediatrics, are out to change that by studying inflammation on a fundamental level.

They'll use a five-year, $3.7 million grant from the National Institutes of Health to examine the onset and resolution of inflammation, work that could point the way to new targeted drug therapies. The grant is funded by the National Institute of Allergy and Infectious Disease.

The researchers will analyze the movement, behavior and communication of neutrophils, the most common type of white blood cell in our bodies, using microfluidic models—an area in which Beebe is a national leader. Neutrophils are part of the innate immune system, the portion of our body's overall defense scheme that responds immediately and uniformly to threats. However, continual neutrophil inflammation can damage tissue and play a role in the chronic inflammation associated with a variety of diseases.

"If we understand this process, then we can say, 'Well if we can tweak this part of the process, we could potentially stop inflammation,'" says Beebe, who notes that the innate immune system has been understudied compared to the adaptive immune system, which crafts cells specifically tailored to each type of invader.

MORE: **www.engr.wisc.edu/new-hope-stopping-understudied-heart-disease-tracks/**

2018 ENGINEERS' DAY AWARD RECIPIENT

Meet our early achiever

Greg Hudalla (MS '06, PhD '10) has quickly established himself as a rising star in biomedical engineering research and education. The assistant professor in the University of Florida's Department of Biomedical Engineering is BME's 2018 Early Career Achievement Award winner as part of the college's annual Engineers' Day celebration.

Hudalla, who studied under Harvey D. Spangler Professor William Murphy, creates functional nano-scale materials for diagnostic or therapeutic applications, particularly around autoimmune diseases, metastasis and viral infections.

The college presented Hudalla with his award during the Engineers' Day banquet in October at the Discovery Building on campus.

Read a Q&A with him: www.engr.wisc.edu/gregory-hudalla-2018-early-career-award-recipient/

FACULTY NEWS

Vilas Distinguished Professor and H.I. Romnes Faculty Fellow **Kristyn Masters** was elected to the American Institute for Medical and Biological Engineering's College of Fellows. She drew praise for her contributions to the design of disease-inspired culture platforms and mentorship of women in STEM fields. Weibo Cai, a BME affiliate, was also elected.

The Harrington Discovery Institute selected Assistant Professor **Krishanu Saha** as a 2018 Gund-Harrington Scholar, citing his work using gene editing nanomedicines to correct retinal mutations. That is the focus of a project that received funding through the Wisconsin Alumni Research Foundation's UW2020 initiative.

Associate Professor **Melissa Skala** is a co-investigator on a UW Carbone Cancer Center and McArdle Laboratory for Cancer Research study backed by a five-year, $3 million grant from the National Cancer Institute. The study, which seeks to advance personalized treatments for colorectal cancer, will use optical imaging techniques that Skala has developed.

Kevin Eliceiri, director of the Laboratory for Optical and Computational Instrumentation in BME, is helping lead a UW-Madison group that's part of the Center for Research in Intelligent Storage and Processing in Memory. The center is funded through a $27.5 million grant from the Semiconductor Research Corporation.

The International Society of Magnetic Resonance in Medicine named Professor **Walter Block** a 2018 fellow of the society.

STUDENT NEWS

Undergraduate student **Will Flanigan** won the best poster award in the cell and developmental biology, immunology and microbiology category at the American Society for Biochemistry and Molecular Biology's 2018 annual meeting in San Diego.

ALUMNI NEWS



Matthew Knoespel (BS '17), **Connor Sheedy** (BS '18) and **Philip Terrien** (BS '17) took first place in the Wisconsin School of Business 2018 Business Plan Competition for the company they helped found, Atrility Medical. They won $4,000 and space in the entrepreneurial base StartingBlock in downtown Madison.

Rebecca Vanderpool (BS '04, PhD '10), an assistant professor at the University of Arizona, became the first woman to win an Early Career Achievement Award from the American Thoracic Society's Pulmonary Circulation Assembly.

Molly Carroll (PhD '17), a postdoctoral researcher in Associate Professor Pamela Kreeger's lab, won the American Association for Cancer Research Scholar-in-Training Award, sponsored by Aflac.

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VEST IS BEST

Nicole Froelich was just starting her first year at UW-Madison in fall 2017, but she had heard about *Interdisciplinary Engineering 170* from a few older friends.

So the BME major knew the introductory design course would expose her and her classmates to working with a client on a tangible project. But she couldn't have possibly guessed that project would lead her more than 8,000 miles from campus the following spring.

"We thought we were just doing a class project," she says.

Yet Froelich and four groupmates found themselves in Kenya in late May 2018, hand delivering the product they had designed in their first-year design practicum: a double-sided vest that will allow women in rural locales to carry water and other goods long distances in a less physically taxing way.

The team, which received a 2018-19 Wisconsin Idea Fellowship, created the vests with a canvas sail donated by the Hoofer Sailing Club at UW-Madison. The plan is for the women to make them using woven-nylon rice bags in the future, ensuring the process is sustainable at the local level and giving them full control over the product.

Photos: Lesley Sager

"Making money is a necessary thing in this day and age," says BME major Jacob Cohn, "but improving other people's lives that are less fortunate is something that isn't valued enough."

MORE: www.engr.wisc.edu/vest-best-students-design-water-carrying-device-rural-kenyans/