

FALL 2017 | BIOMEDICAL ENGINEERING

FROM BLACK-EYED PEAS TO NANOTECHNOLOGY

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A joint department between the Case School of Engineering
and Case Western Reserve University School of Medicine

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EXPLORE

Biomedical Engineering at Case Western Reserve University

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FROM THE CHAIR



It is my pleasure to present to you this newsletter highlighting some of the activities happening in the highly dynamic Department of Biomedical Engineering at Case Western Reserve University, where I have the honor to serve as Chair. I am constantly amazed at the creativity and energy exhibited by our faculty and students as they pursue myriad activities. Our biomedical engineering department turns 50 years old next year, and the stability, rigor and culture of excellence that time has allowed is clearly evident in our department today. As examples, did you know:

- **Our department is home to 110 faculty members?** With 30 primary faculty members and 80 associated faculty members, we are one of the larger biomedical engineering departments nationally!
- **We are a joint department between the Case School of Engineering and the Case Western Reserve School of Medicine?** We operate seamlessly and effectively in this very rich and collaborative environment.
- **We have been an educational leader in biomedical engineering for 50 years and continue to innovate these programs?** We currently have 500 undergraduate, 80 M.S. and 100 Ph.D. students.
- **Our department is home to one of the original, endowed Coulter Translational Research Partnerships?** This program has produced multiple licenses and startups and more than 20 “first in man” medical products, and has helped engender an exciting entrepreneurial environment in Cleveland.
- **Case Western Reserve University is surrounded by an incredible medical environment?** Biomedical engineering is a hub for research, with faculty maintaining laboratories and collaborations with all four of our medical affiliates (University Hospitals, Cleveland Clinic, Louis Stokes Cleveland VA Medical Center, MetroHealth Medical Center).

However, the Case Western Reserve biomedical engineering program has never rested on its laurels. As you will see in this newsletter, we continue to innovate and lead in education, research and entrepreneurship. Our faculty pursue research in new and exciting areas, publish (usually with their student trainees!) in the best journals and are strongly funded to pursue visionary, paradigm-shifting research. Our faculty are leaders in the field, organizing many influential international conferences each year and leading important national groups – for example, I am Chair of the National BME Council of Chairs this year. Our students and alumni thrive in industry, academia, and medicine – and even become department chairs!

Please enjoy this update, and feel free to contact me at any time!

Robert F. Kirsch, PhD

Allen H. and Constance T. Ford Professor
Chair of Biomedical Engineering
Case Western Reserve University

BY THE NUMBERS: BIOMEDICAL ENGINEERING FUNDING

funding from

>50 institutions
including 12 NIH Institutes

half of primary faculty

>\$500,000 NIH funding

Statistics provided by NIH Reporter

FACULTY HIGHLIGHTS



FACULTY LAND LEADING ROLES AT GORDON RESEARCH CONFERENCES

Gordon Research Conferences (GRC) organizes more than 365 international conferences dedicated to advancing scientific research in biological, chemical and physical sciences, as well as their related technologies. Each prestigious conference is limited to 200 attendees, who must apply to the conference and be selected by the conference chair to attend the meeting. Together, attendees strive to advance the frontier of the field.

Since 2015, three faculty members in the Biomedical Engineering department have been named conference chairs by GRC:



Nicole Steinmetz

2015 Chair of the Physical Virology GRC

In January 2015, Nicole Steinmetz, associate professor of biomedical engineering in the Case Western Reserve University School of Medicine, co-chaired the Physical Virology GRC. The focus of the conference was "Integrating Global Significance with Atomic Level Understanding."



Horst von Recum

2017 Chair of the Biomaterials & Tissue Engineering GRC

In July, Horst von Recum, a professor of biomedical engineering, co-chaired the conference on "Building Novel Molecular Designs and Basic Biological Discoveries into Successful Medical Technologies." A group of world-class clinicians, scientists and engineers discussed materials-related strategies for disease remediation and tissue repair.



Jeffrey Capadona

2018 Chair of the Neuroelectronic Interfaces GRC

The conference, entitled "Beyond Feasibility – Bridging the Gap in Neuroelectronic Interfaces," will be held March 25-30, 2018, in Galveston, Texas. Capadona, an associate professor of biomedical engineering, was selected to co-chair this inaugural GRC conference, which will bring together a multidisciplinary team of experts in cellular neuroscience, brain pathology, neuro-technology and materials science to discuss obstacles on the quest for a useful and reliable neural interface.

POSTDOC CHAIRS GORDON RESEARCH SEMINAR



Jenny Parvani

2017 Chair of the Gordon Research Seminar on Hormone-Dependent Cancers

Jenny G. Parvani, a postdoctoral fellow in the Biomedical Engineering Department, chaired the Gordon Research Seminar on Hormone-Dependent Cancers in August. She also won a poster award at the event for her work exploring the mechanism of Oncostatin-M mediated chemoresistance in triple negative breast cancer.

BIOMEDICAL ENGINEERING ENDOWED PROFESSORSHIPS

An endowed professorship is among the highest honors a member of the university faculty can receive. The appointment reflects the institution's appreciation of a scholar's achievements and provides essential support to advance additional intellectual work. In 2017, three faculty members in the Biomedical Engineering Department were named endowed professors:



Anant Madabhushi

F. Alex Nason Professor II



Nicole Seiberlich

Elmer Lincoln Lindseth

Associate Professor



Dustin Tyler

Kent H. Smith Professor

of Engineering II

THREE BIOMEDICAL ENGINEERING PROJECTS OBTAIN I-CORPS@OHIO FUNDING

I-Corps@Ohio recently awarded funding to three projects led by faculty at Case Western Reserve's Department of Biomedical Engineering. Modeled after the National Science Foundation's I-Corps program, the main goal of the statewide grant-funded program is to accelerate commercialization of technologies developed at Ohio universities.

Biomimetic, Antioxidative Coatings For Neural Implants



A team led by Jeffrey Capadona has developed a coating technology for medical devices aimed at mitigating deleterious oxidative stress events that lead to device failure. Through the I-Corps@Ohio program, the team hopes to develop a platform for applying this coating to a variety

of neural implants to improve functionality and increase long-term device stability. Biomedical engineering graduate student Griffin Rial and post-doc Andrew Shoffstall are co-entrepreneurial leads on the project.

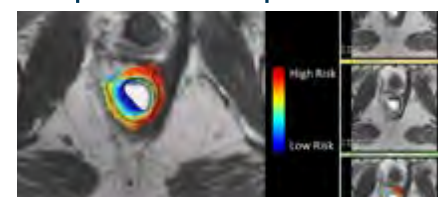
An Enzyme Biomarker Analyzer



Miklos Gratzl serves as principal investigator on a project aimed at commercialization of proprietary intellectual property for measuring nearly 50 percent of all clinically important enzyme markers in point-of-care settings using disposable slides and one device. His team in the Laboratory for Biomedical Sensing has created an enzyme biomarker analyzer based on micro-pH-stating for point-of-care diagnostics of many acute diseases and chronic conditions.

Zhehao Zhang, a graduate student in biomedical engineering, is entrepreneurial lead on the project.

Computational Scalpel™



A team led by Satish Viswanath has developed a patented machine learning-based surgical planning tool for use by colorectal surgeons. The technology constructs a precise GPS-style surgical margin plan that provides a high-resolution, interactive visualization of tumor extent in vivo on rectal MRIs. This will allow colorectal surgeons to plan procedures to be as minimally invasive as possible while improving patient outcomes and reducing recurrence rates. Jacob Antunes, a graduate student in biomedical engineering, serves as entrepreneurial lead.

RESEARCHERS SECURE GRANT FUNDING

Anirban Sen Gupta



Photo by Russell Lee

Anirban Sen Gupta, associate professor of biomedical engineering, received a grant award from the Defense Medical Research and Development Program (DMRDP) under the Department of Defense to evaluate synthetic platelet-

based technologies for mitigation of hemorrhage control and treatment of burn wounds in large animal polytrauma models. This work will be carried out in collaboration with the University of Pittsburgh Department of Surgery (collaborator: Matthew Neal) and U.S. Army Institute of Research, San Antonio (collaborator: Rodney Chan).

Sen Gupta is also a co-investigator on an American Heart Association National Grant-in-Aid award funded in 2017 to Michael Suster (PI) and Pedram Mohseni (Co-I) of the Department of Electrical Engineering and Computer Science at Case Western Reserve to develop and evaluate a dielectric microsensor for point-of-care analysis of hemostatic defects.



Horst von Recum



Horst von Recum, professor of biomedical engineering, received an R01 grant for his project entitled, "Reducing Adhesions in Hernia Repair Meshes Through a Polysaccharide Coating" from the National Institute of General Medical Services at the National Institutes of Health. Through his research, von Recum will create a family of polysaccharide-based polymers to coat hernia repair meshes, mimicking the anti-adhesive properties of the endothelial glycocalyx. Preliminary data both in vitro and in rodent

and pig models have shown this strategy to reduce adhesions beyond that of uncoated meshes.

The five-year grant will be utilized to assess the range of polysaccharide chemistries capable of preventing adhesions, while retaining mesh repair durability and cell adhesion. The long-term goal of von Recum's research is to develop a low-cost, biocompatible device coating that can prevent or reduce post-surgical adhesions following hernia repair.

CLINICAL TRIAL SPOTLIGHT



Photo by Russell Lee, © Case Western Reserve University and Cleveland FES Center

MAN WITH QUADRIPLÉGIA EMPLOYS INJURY BRIDGING TECHNOLOGIES TO MOVE AGAIN — JUST BY THINKING

First recipient of implanted brain-recording and muscle-stimulating systems reanimates limb that had been stilled for eight years.

Bill Kochevar grabbed a mug of water, drew it to his lips and drank through the straw. His motions were slow and deliberate, but then Kochevar hadn't moved his right arm or hand for eight years. And it took some practice to reach and grasp just by thinking about it.

Kochevar, who was paralyzed below his shoulders in a bicycling accident, is believed to be the first person with quadriplegia in the world to have arm and hand movements restored with the help of two temporarily implanted technologies. A brain-computer interface with recording electrodes under his skull, and a functional electrical stimulation (FES) system* activating his arm

and hand, reconnect his brain to paralyzed muscles.

Holding a makeshift handle pierced through a dry sponge, Kochevar scratched the side of his nose with the sponge. He scooped forkfuls of mashed potatoes from a bowl — perhaps his top goal — and savored each mouthful. "For somebody who's been injured eight years and couldn't move, being able to move just that little bit is awesome to me," says Kochevar, 56, of Cleveland. "It's better than I thought it would be."

Kochevar is the focal point of research led by Case Western Reserve University, the Cleveland Functional Electrical Stimulation (FES) Center at the Louis Stokes

Cleveland VA Medical Center and University Hospitals Cleveland Medical Center. A study of the work was published in the *The Lancet* on March 28, 2017.

"He's really breaking ground for the spinal cord injury community," says Robert Kirsch, chair of Case Western Reserve's Department of Biomedical Engineering, executive director of the FES Center, principal investigator, and senior author of the research. "This is a major step toward restoring some independence."

When asked, people with quadriplegia say their first priority is to scratch an itch, feed themselves or perform other simple functions with their arm

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online-engineering.case.edu/biomedical



and hand, instead of relying on caregivers. “By taking the brain signals generated when Bill attempts to move, and using them to control the stimulation of his arm and hand, he was able to perform personal functions that were important to him,” says Bolu Ajiboye, assistant professor of biomedical engineering and lead study author.

Technology and Training

The research with Kochevar is part of the ongoing BrainGate2* pilot clinical trial being conducted by a consortium of academic and VA institutions assessing the safety and feasibility of the implanted brain-computer interface (BCI) system in people with paralysis. Other investigational BrainGate research has shown that people with paralysis can control a cursor on a computer screen or a robotic arm. Learn more at braingate.org.

“Every day, most of us take for granted that when we will ourselves to move, we can move any part of our body with precision and control in multiple directions and those with traumatic spinal cord injury or any other form of paralysis cannot,” says Benjamin Walter, associate professor of neurology at Case Western Reserve School of Medicine, clinical PI of the Cleveland BrainGate2 trial and medical director of the Deep Brain Stimulation Program at UH Cleveland Medical Center. “The ultimate hope of any of these individuals is to restore this function,” Walter says. “By restoring the communication of the will to move from the brain directly to the body, this work will hopefully begin to restore the hope of millions of paralyzed individuals that someday they will be able to move freely again.”

Jonathan Miller, assistant professor of neurosurgery at Case Western Reserve School of Medicine and

director of the Functional and Restorative Neurosurgery Center at UH, led a team of surgeons who implanted two 96-channel electrode arrays — each about the size of a baby aspirin — in Kochevar’s motor cortex, on the surface of the brain. The arrays record brain signals created when Kochevar imagines movement of his own arm and hand. The brain-computer interface extracts information from the brain signals about what movements he intends to make, then passes the information to command the electrical stimulation system.

To prepare him to use his arm again, Kochevar first learned how to use his brain signals to move a virtual-reality arm on a computer screen. “He was able to do it within a few minutes,” Kirsch says. “The code was still in his brain.”

As Kochevar’s ability to move the virtual arm improved through four months of training, the researchers believed he would be capable of controlling his own arm and hand.

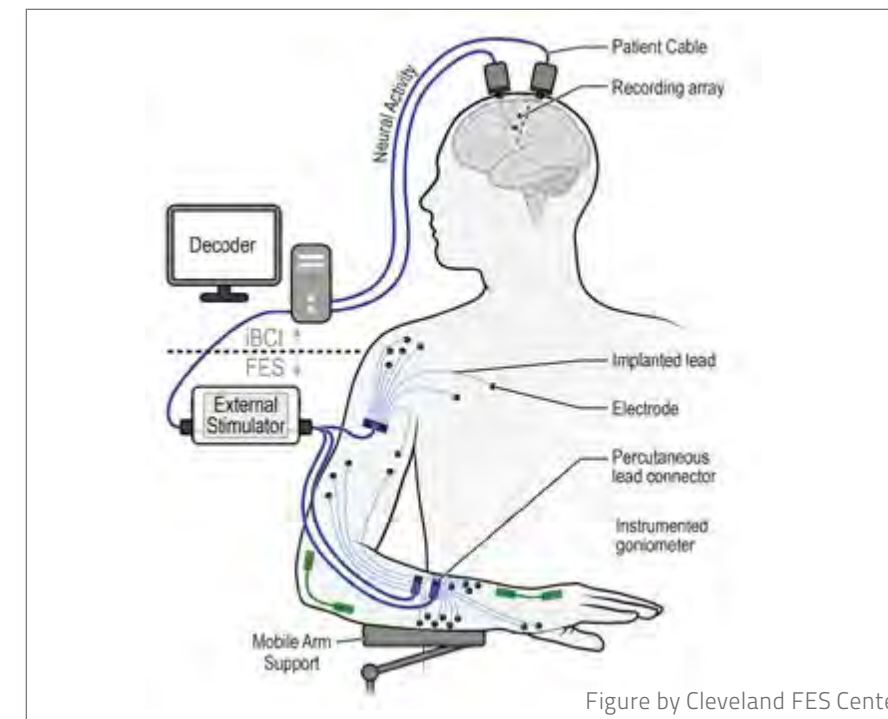
Miller then led a team that implanted the FES systems’ 36 electrodes that animate muscles in the upper and lower arm. The BCI decodes the recorded brain signals into the intended movement command, which is then converted by the FES system into patterns of electrical pulses. The pulses sent through the FES electrodes trigger the muscles controlling Kochevar’s hand, wrist, arm, elbow and shoulder. To overcome gravity that would otherwise prevent him from raising his arm and reaching, Kochevar uses a mobile arm support, which is also under his brain’s control.

New Capabilities

Eight years of muscle atrophy required rehabilitation. The researchers exercised Kochevar’s arm and hand with cyclical

“He’s really breaking ground for the spinal cord injury community. This is a major step toward restoring some independence.”

- Robert Kirsch



electrical stimulation patterns. Over 45 weeks, his strength, range of motion and endurance improved. As he practiced movements, the researchers adjusted stimulation patterns to further his abilities.

Kochevar can make each joint in his right arm move individually. Or, just by thinking about a task such as feeding himself or getting a drink, the muscles are activated in a coordinated fashion.

When asked to describe how he commanded the arm movements, Kochevar tells investigators, “I’m making it move without having to really concentrate hard at it... I just think ‘out’... And it goes.”

Kochevar is fitted with temporarily implanted FES technology that has a track record of reliable use in people. The BCI and FES system together represent early feasibility that gives the research team insights into the potential future benefit of the combined system.

Advances needed to make the combined technology usable outside of a lab are not far from reality, the researchers say. Work is underway to make the brain implant wireless, and the investigators are improving decoding and stimulation patterns needed to make movements more precise. Fully implantable FES systems have already been developed and are continuing to be tested in separate clinical research. Kochevar welcomes new technology — even if it requires more surgery — that will enable him to move better. “This won’t replace caregivers,” he says. “But, in the long term, people will be able, in a limited way, to do more for themselves.”

The investigational BrainGate technology was initially developed in the Brown University laboratory of John Donoghue, now the founding director of the Wyss Center for Bio and

Neuroengineering in Geneva, Switzerland. The implanted recording electrodes are known as the Utah array, originally designed by Richard Normann, Emeritus Distinguished Professor of Bioengineering at the University of Utah. The report in *The Lancet* is the result of a long-running collaboration between Kirsch, Ajiboye and the multi-institutional BrainGate consortium.

Leigh Hochberg, MD, PhD, a neurologist and neuroengineer at Massachusetts General Hospital, Brown University and the VA RR&D Center for Neurorestoration and Neurotechnology in Providence, R.I., directs the pilot clinical trial of the BrainGate system and is a study co-author.

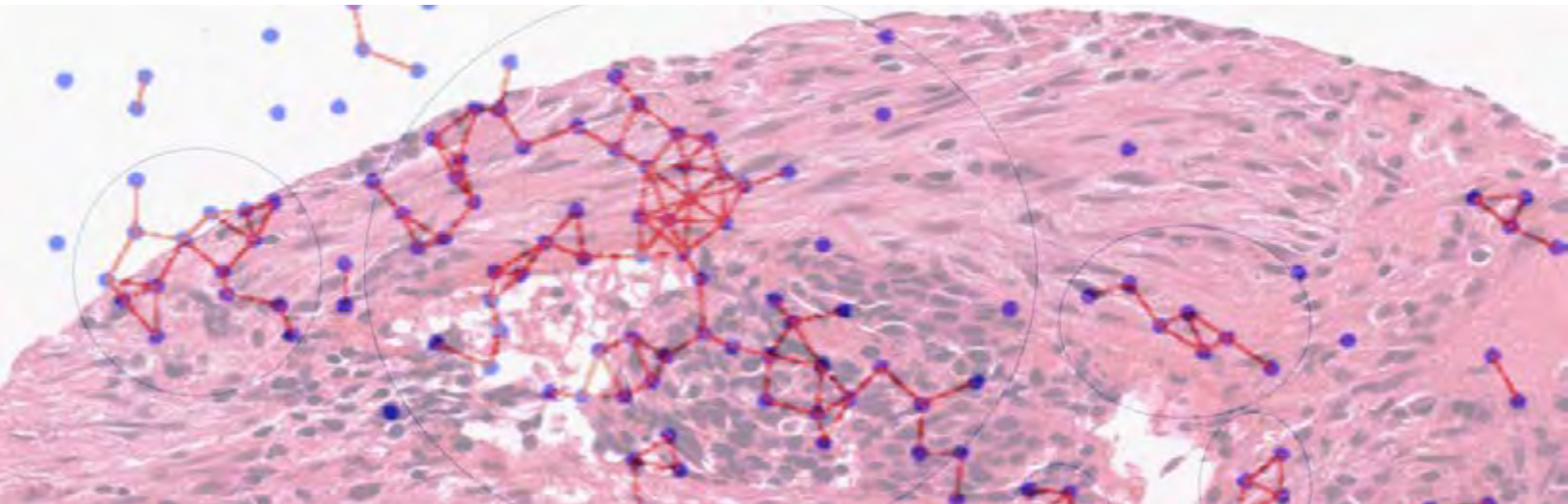
“It’s been so inspiring to watch Mr. Kochevar move his own arm and hand just by thinking about it,” Hochberg says. “As an extraordinary participant in this research, he’s teaching us how to design a new generation of neurotechnologies that we all hope will one day restore mobility and independence for people with paralysis.”

Other researchers involved with the study include: Francis R. Willett, Daniel Young, William Memberg, Brian Murphy, PhD, and P. Hunter Peckham, PhD, from Case Western Reserve; Jennifer Sweet, MD, from UH; Harry Hoyen, MD, and Michael Keith, MD, from MetroHealth Medical Center and CWRU School of Medicine; and John Simeral, PhD, from Brown University and Providence VA Medical Center.

*CAUTION: Investigational Device. Limited by Federal Law to Investigational Use.

Learn more at BrainGate2.case.edu

FEATURED LAB



MINING DATA FOR MEDICAL BREAKTHROUGHS

Researchers at the Center for Computational Imaging and Personalized Diagnostics use imaging data to create predictive models that can aid disease management and treatment.

On a picturesque evening in July, Pallavi Tiwari headed to the Sunflower Soiree in downtown Cleveland. Like other attendees, she listened to music and feasted on an array of food prepared by local restaurants. While the night was festive, it had a higher purpose — to raise money for Prayers from Maria, the Children’s Glioma Cancer Foundation, named in memory of Maria McNamara, who died from the disease in 2007 at age seven.

Tiwari, a School of Medicine assistant professor of biomedical

engineering at Case Western Reserve University at the Center for Computational Imaging and Personalized Diagnostics (CCIPD), has spent the past four years developing neuroinformatics techniques for evaluating the presence of brain tumors and response to treatment of the disease. Although professional interest drove her to the Sunflower Wine Festival, the evening quickly became personal.

“Working in the center, we don’t regularly interact with patients,”

says Tiwari. “But I met patients, parents and family at the fundraising event. They told stories about living with gliomas, and it hit home for me. I need to do whatever I can to make sure there is something out there that can help these children.”

Tiwari’s contribution to fighting brain tumors utilizes automated algorithms to analyze and integrate multi-modal imaging data for disease diagnosis, prognosis and treatment evaluation. The project that has made the most progress

to date involves the latter. “Brain tumor patients get aggressive chemo radiation,” says Tiwari. “When they come back for follow-up MRIs, many times clinicians see enhancements on the images that look like the tumor has come back. However, sometimes it’s just a side effect of the aggressive radiation.” Typically, clinicians perform a biopsy to determine if it’s a tumor or benign side effect.

Tiwari and a team of a dozen undergraduates, graduate students and postdoctoral researchers in the CCIPD have accrued and evaluated more than 200 retrospective studies from multiple medical centers across the United States and China. Using machine learning, statistical modeling and pattern recognition, they are close to 90 percent accurate distinguishing between tumors and benign side effects — almost twice as accurate compared with neuroradiologists who read the same studies. If clinicians know exactly what they are dealing with, they can better treat patients.

The work continues thanks to a grant from the Ohio Third Frontier Technology Validation and Start-up Fund. “The results look very promising,” says Tiwari. “What we want to do next is take the technology, deploy it in a clinical setting and see how well it does.”

Extracting Value from Imaging Data

Tiwari is one of five faculty working

together with about 35 other staff members, research associates, students and interns at the CCIPD, which was founded in 2012 by Anant Madabhushi, the F. Alex Nason II Professor of biomedical engineering at Case Western Reserve University. “Our main goal, in the simplest terms, is to try to extract as much value as possible from imaging data to facilitate patient management and treatment,” says Madabhushi.

The CCIPD currently focuses on four broad subject areas: image-guided interventions, digital pathology, machine learning and personalized medicine, and computational diagnostics. One overarching goal is to use imaging data to better predict the aggressiveness of a disease and the appropriate treatment for individual patients — to push the needle in terms of precision medicine.

In just five years, the center has been quite successful. The three primary faculty — Madabhushi, Tiwari and Satish Viswanath, assistant professor of biomedical engineering in the Case Western Reserve University School of Medicine — have more than 50 patents issued or pending related to their research. In the two-year period between September 2015 and September 2017, researchers in the CCIPD have received in excess of \$13 million in total funding.

Joining the three primary faculty members in the center are two affiliated faculty, David Wilson, the Robert J. Herbold professor

“Individually, everyone involved does great work. They are experienced researchers and clinicians, but the sum of the parts is greater than any individual.”

— Satish Viswanath

of biomedical engineering, and Vinay Varadan, assistant professor of general medical sciences (oncology) in the Case Comprehensive Cancer Center. Wilson focuses cardiovascular diseases, with recent highlights of his research including coronary plaque imaging using intravascular optical coherence tomography (OCT), detection of cardiac ischemia using CT and detection of coronary calcium using low-cost chest X-rays. Varadan is developing and applying multi-scale systems biology approaches to delineate mechanisms of disease progression and discover novel biomarkers of therapy response in cancer.

While the team has worked on a variety of diseases, ranging from epilepsy to digestive diseases, the mainstay of its research pertains to cancer for two primary reasons — one that’s altruistic, and the other more practical. “Cancer conjures up a fear that perhaps no other disease does in quite the same way,” says Madabhushi. “On a more practical note, the fact is for what we do, data is king. And the cancer space has a long history of carefully recording data and capturing outcomes, which we can use to create predictive models to figure out how these patients are going to do and respond to treatment.”

For data scientists, says Madabhushi, that’s a good place to be. “A critical piece in all the models we create is how did the patient do?” he says. “If you don’t have that information, then you can’t really do much.” Knowing patient outcomes is key to evaluating predictive models.

Although cancer organizations lead the way on the big data front, others are catching up. For instance, the National Institute of Diabetes and Digestive Diseases

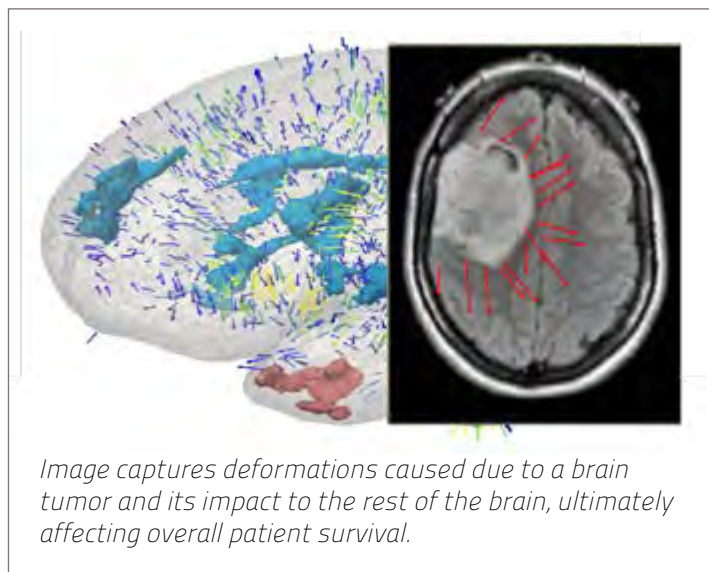


Image captures deformations caused due to a brain tumor and its impact to the rest of the brain, ultimately affecting overall patient survival.

and Kidney Disorders has called for precision medicine initiatives inspired by the cancer community. “As the infrastructure evolves and the data sets and outcome information become available,” says Madabhushi, “there’s no doubt in my mind that we will start to take our bag of tools and apply it to other indications.”

Collaborating with Clinicians

Collaboration among disciplines

is key to the work conducted at the CCIPD. “We need to bring together information from across multiple modalities — MRIs, genetic tests and so on,” says Viswanath. “And the best way to get an understanding of what each modality is capturing is by engaging different people.”

Viswanath’s research on colorectal cancer illustrates the importance of interdisciplinary teamwork. In 2016, he was awarded a three-year, \$569,000 grant from the

Department of Defense’s Congressionally Directed Medical Research Programs for a colorectal cancer project. “This project is unique because it brings together a variety of disciplines from three different medical institutions – University Hospitals, Cleveland Clinic and the VA Medical Center,” says Viswanath. A team of pathologists, radiologists,

biostatisticians and colorectal surgeons are partnering with Viswanath and Madabhushi, co-investigator on the project, as well as Dr. Sanford Markowitz, who holds the Markowitz-Ingalls professorship of Cancer Genetics at Case Western Reserve University School of Medicine. “Individually, everyone involved does great work. They are experienced researchers and clinicians,” says Viswanath. “But the sum of the parts is greater than any individual.”



From left: Pallavi Tiwari, Satish Viswanath and Anant Madabhushi working with students

The group is developing new image analytics tools to guide treatment and therapeutic interventions in colorectal cancer patients using standard-of-care imaging. “There’s an opportunity to build new tools and provide people with the information they need to potentially avoid surgeries and plan follow-up treatments,” says Viswanath. This would be particularly helpful for colorectal cancer, where it’s difficult to identify the extent and aggressiveness of the disease — or if it’s regressed after treatment.

The project includes two components. The first is a surgical “GPS” plan using analytic tools that provide a map — or navigation system — for honing surgery. If clinicians had a more accurate visualization of the extent of the tumor, they could potentially customize the surgery to the patient rather than perform a complete colorectal excision. The second component is development of a risk scoring system to identify the magnitude of a patient’s disease, then provide a risk stratification score to determine if treatment or a “wait and watch” approach is necessary.



Madabhushi calls the CCIPD’s close proximity to major medical centers in Cleveland “a game changer.” He often schedules one-on-one meetings with leading physicians in breast cancer — one of his research focus areas — and takes students with him. “It’s absolutely fabulous for the students,” he says. “The ability to get immediate, translatable feedback from clinicians is huge. You can’t buy that.”

Creating Collegiality in the Lab

Just as the CCIPD fosters collaboration with clinicians, so too does it emphasize teamwork among colleagues in the center. “We have close to 40 people working on different projects, but because we meet so regularly everyone knows what the others are working on,” says Tiwari. “We help each other out whenever we can.”

One way Madabhushi encourages camaraderie is through the Friday Literary Guild, a practice he started as a professor at Rutgers University in 2005 and continues today at Case Western Reserve University. The CCIPD team is enticed to the weekly meeting through the

promise of lunch, then they share status reports on their projects and present research papers. The Friday Literary Guild is approaching its 400th meeting.

“It’s critical to get everybody in the same room, listening to different people present,” says Madabhushi. “It’s very easy for a student to think about his or her particular thesis project and stay in that silo. I understand that, because you have to drill deep. But if you shut off all that’s going on around you, that’s counterproductive. Good ideas may come from another area.”

It’s all about creating synergies — between projects and people. “At the center, we have people in different disciplines looking at different diseases from different perspectives. We are doing disease diagnosis, prediction, prognosis, prevention and treatment,” says Viswanath. “We can attack problems from so many perspectives. When you begin to look at problems holistically, you see connections you might not have seen previously.”

Ultimately, those connections will benefit clinicians and their patients. Patients like Maria McNamara.

COVER STORY

FROM BLACK-EYED PEAS TO NANOTECHNOLOGY

The Steinmetz Lab advances medicine and materials through molecular engineering of bio-inspired nanotechnologies.

Plants are frequently used in biomedical research. One of the most publicized recent success stories is the development of ZMapp™, an experimental therapy to treat Ebola Virus Disease. Created by a team of scientists, the intravenous treatment is composed of three monoclonal antibodies manufactured in *Nicotiana benthamiana*, commonly known as Australian tobacco.

Nicole Steinmetz, an associate professor of biomedical engineering and the George J. Picha Designated Professor in Biomaterials at the Case Western Reserve University School of Medicine, also uses Australian tobacco to push frontiers in medicine and materials through molecular engineering of biology-inspired nanotechnologies. However, there's a twist. "Many labs use nanotechnology for human or plant health

applications," says Steinmetz. "Our unique angle is that we use plant viruses."

Founded in 2010, the Steinmetz Lab studies and applies plant viruses generated from Australian tobacco and black-eyed peas



to manufacture nanoparticles to cure diseases. "The interest lies in the nanometer size scale because these materials

can navigate through the body in ways other materials can't," says Steinmetz, principal investigator in the lab.

Nanoscale self-assembly has been mastered in nature with atomic precision. Rather than synthesize nanoparticles in the lab, researchers in the Steinmetz Lab use biology to make nanomaterials for them. Viruses also offer distinct characteristics

that the researchers capitalize on: They have naturally evolved to deliver cargos to cells and tissues. "Through structure-function studies, we are beginning to understand how to tailor these materials appropriately for applications in medicine and biotechnology," says Steinmetz.

The team in the Steinmetz Lab includes two research professors, a lab manager and more than a dozen postdoctoral fellows and graduate students. Their work is organized into three interconnected research thrusts:

- Drug delivery and immunotherapies
- Molecular imaging for diagnosis and prognosis
- Synthetic virology approaches toward novel materials

A Focus on Plant Viruses

Steinmetz's interest in bio-inspired approaches to fighting



Photo by Russell Lee

disease was sparked early on. In the late 1990s, she was a biology student at the Ruhr University Bochum in Germany majoring in biology. "I enjoyed learning about biology and how it works, but I always wanted to do something more applied — use biology to make a new material, cure a disease or make a vaccine," she says.

Because of her interests in applied biology, Steinmetz continued her studies in molecular biotechnology at the RWTH Aachen University in Germany. While there, she heard a lecture by Dr. Ulrich Commandeur.

"He was using plant viruses to produce antibodies in plants to make them more accessible to the developing world," recalls Steinmetz. "You could eliminate the cold chain and produce pharmaceuticals in plants on site. That was really cool!" Shortly afterward, Steinmetz joined the Commandeur Lab to start her diploma (equivalent to a master's thesis) in molecular farming with plant viruses.

Plant viruses are the center — the nucleus — of all the work done in the Steinmetz Lab. Two common viruses the researchers utilize are

tobacco mosaic virus and cowpea mosaic virus. In a new lab in the basement of the Biomedical Research Building on the School of Medicine's campus, researchers grow a couple hundred Australian tobacco and black-eyed pea plants.

"Once they grow to a certain size, we infect them by putting a drop of the virus on the leaves and rubbing it in. It's very simple," says Frank Veliz, lab manager of the Steinmetz Lab. "We continue to water the plants and let them grow. Then, over time, the plants start to show a mosaic pattern on the leaves." At that point, the



Once grown to the appropriate size, the plants are infected with the virus by putting a drop on the leaf and rubbing it in.

leaves are harvested, undergo a purification process and are ready for use in the main facility of the Steinmetz Lab on the third floor of the Biomedical Research Building. Whether for drug delivery, immunotherapy or molecular imaging, the basic concept remains the same. "The whole idea is that you want a cargo — either your drug or your contrast agent — to specifically deliver to the site of the disease," says Steinmetz. Researchers create a hollow nanotube, akin to an incredibly small paper towel roll. The interior is solvent accessible, so a drug or contrast agent in solution can freely diffuse on the inside. Chemistries are then used to trap the drug or contrast agent on the inside. The exterior of the nanotube

is modified to provide direction on where it should go within the body — what Steinmetz calls "molecular ZIP codes." One of the potential applications for this technology is risk stratification for cardiovascular disease. Non-invasive imaging techniques can help improve survival and quality of life, as well as reduce healthcare costs. While MRI is beneficial, it's limited in its ability to distinguish between diseased and healthy tissue of similar signal intensities. Researchers at the Steinmetz Lab developed molecularly targeted nanoscale contrast agents carrying large payloads of the clinically approved agent Gd-DOTA. The contrast agent, which uses the nucleoprotein components of the tobacco mosaic virus, exhibits a

relaxivity five orders of magnitude higher than current clinical agents. Using plant virus nanotubes, the team identified novel biomarkers and their peptide ligands to differentiate between vulnerable and stable plaque. Ultimately, this could help physicians decide which patients require treatment and what treatment is most suitable.

A Promising Approach to Immunotherapy

Steinmetz says the most exciting research area in the lab right now — and the one that's closest to translation — is cancer immunotherapy. "The contemporary approach in nanomedicine is to take a nanocarrier, put a drug inside and deliver the drug to the site of the disease to help position the chemotherapy more toward the tumor," she says. "Ours is a completely different approach. We seek to interact with the body's immune system and train it to recognize the tumor."

The immune system defends the body against cancer by sending T-cells to find and kill tumor cells. Over time, however, the tumor shuts down the immunity cycle and tumors become immunosuppressive. The Steinmetz Lab recently demonstrated that virus-like particles (VLPs) from plants induce a potent anti-tumor immune response when introduced into the tumor microenvironment after tumors are established.

The researchers have termed their proteinaceous plant virus-derived

nanocarriers an "in situ vaccine." When injected directly into the tumor, the therapy manipulates tumors to overcome local tumor-mediated immunosuppression and subsequently stimulate systemic anti-tumor immunity to treat metastases. It is both a cancer treatment and a preventive measure against future tumor growth. The Steinmetz Lab has demonstrated efficacy of the in situ vaccine in melanoma, ovarian, colon, glioma and breast tumor models.

In collaboration with Steven N. Fiering, professor of microbiology and immunology, and P. Jack Hoopes, a veterinarian and professor of surgery and radiation oncology at the Dartmouth Geisel School of Medicine, Steinmetz has tested the therapy on four dogs with highly malignant oral melanoma. The dogs were treated with standard clinical radiation therapy (RT) and intra-tumor VLP. Radiation therapy alone provides an average disease-free survival of nine months in these patients. Currently none of four RT/VLP treated melanomas has recurred locally or metastasized. The ongoing average disease-free survival is now at 12 months, and the tumor/peri-tumor influx of cytotoxic immune cells is more than three-fold greater than is seen with radiation alone.

"We are just scratching the surface with immunotherapy," says Steinmetz. "We have something that works in large animals, so we want to push this toward a clinical trial. But there's still a lot

"Many labs use nanotechnology for human or plant health applications. Our unique angle is that we use plant viruses."

— Nicole Steinmetz

of research to be done." Her team is further studying the molecular mechanism and how to make it more potent. They are also looking at combining the therapy with other drugs, formulating it into slow release devices and trying different routes of injection.

A Bright Future

The work done in the Steinmetz Lab is being expanded to another facility on the Case Western Reserve campus, the new Center for Bio-Nanotechnology. Steinmetz is director of the center, which opened in July. "The idea is to bring different principal investigators and labs together to build on different technologies

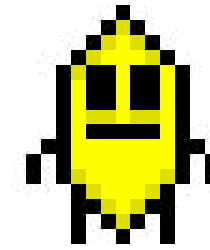
to attack the same problems," she says. While her team utilizes plant viruses, others have made advancements with different materials. Together, researchers ranging from nanotechnologists to cell biologists and clinicians can work on common goals.

Such collaboration appeals to researchers in the Steinmetz Lab. "What I really like about our lab is that we work well together," says Veliz. "We collaborate not just with each other, but with other labs on campus for a lot of our projects. We turn to people with the required expertise."

The work done by Steinmetz has garnered attention — and

funding. Earlier this year, she received three new major grants from the National Institutes of Health to further develop her immunotherapy approach, as well as to further study drug-delivery systems for patients living with triple-negative breast cancer and those at risk for serious blood clots. The two R01 awards and one U01 award total more than \$8.5 million.

"If this therapy really translates well in human patients — the immunotherapy in particular — not only will we have a treatment, but also a vaccine that would prevent recurrence of the disease," says Steinmetz. "That's what I'm most excited about."



THE NANOMAN

Just as Nicole Steinmetz was inspired by a college professor to move into bio-based research, so too would she like to influence the next generation of researchers.

The associate professor of biomedical engineering teamed with Knight & Brinegar, a retro-forward writing team, to create the Nanoman multimedia outreach program.

The Nanoman program's mission is to disseminate recent scientific advances in the area of nanotechnology and oncology to the general public and K-12 students. The program combines nanoscience and technology with live musical theater, animated video, gaming and a website at www.thenanoman.org. Steinmetz and her partners have already produced "The Nanoman: An Interactive Nerdcore Musical," which ran in New York and Berkeley, Calif. The theatrical event follows mad scientist Dr. X as she battles a tumor using the Nanoman, a plant virus transformed into

a biomolecular engineered nanocarrier. The Nanoman is a tiny superhero on an important mission — to locate and destroy the tumor.

The Nanoman also makes star appearances in multimedia games and YouTube videos. In one video, Dr. X sings:

"I needed a virus, one I could control, but I couldn't seem to find one around.

Then I thought — plants! And I'm here to show you the formula that I found."

In the campy music video, Dr. X goes on to talk about virus propagation, purification, bioconjunction and characterization.

Tongue-in-cheek? Sure. But the Nanoman makes science — and drug delivery therapies in particular — accessible to the next generation of researchers. And who knows what contributions they may make to the biomedical field.

For videos and more information, visit:

thenanoman.org



COLLABORATIONS

CLEVELAND: A POWERHOUSE FOR PARTNERSHIPS

Collaboration among researchers, clinicians and industry is key to success in biomedical engineering. Case Western Reserve University's Department of Biomedical Engineering is fortunate to be located in the heart of Cleveland, a global center for health innovation. It's surrounded by four major hospital systems — Cleveland Clinic, MetroHealth, University Hospitals, and the Louis Stokes Cleveland VA Medical Center. In addition, there are more than 700 biomedical companies in northeast Ohio, according to The Medical Capital Initiative convened by BioEnterprise.

Such close proximity to a wide variety of biomedical organizations yields fruitful partnerships. "Cleveland is often underappreciated in terms of how much of a powerhouse it is for biomedical research,"

says Vamsidhar Velcheti, a Professor of Medicine at the Cleveland Clinic Lerner College of Medicine and staff physician in the Department of Hematology and Oncology at Cleveland Clinic Taussig Cancer Center. "You have world-class medical institutions here, and at the same time you have access to some of the best minds at Case Western Reserve University — especially in biomedical engineering. It provides for a scientifically stimulating environment."

Velcheti, who specializes in lung cancer, has teamed up with Anant Madabhushi for several years. Madabhushi is a professor of biomedical engineering at Case Western Reserve University and director of the Center of Computational Imaging and Personalized Diagnostics.

Together, they are researching effective ways of quantifying and predicting early response to targeted therapies for lung cancer using radiographic analysis of CT scans and histomorphometric analysis of tissue images.

"I have a lot of interest in translational research and biomarkers to identify patients who would benefit from certain treatments," says Velcheti. "Collaborating with someone like Dr. Madabhushi presents a great opportunity to advance science and create new diagnostic tools to help better assist our patients in getting the right treatments."

The project between Madabhushi and Velcheti is just one of many researcher/clinician partnerships fostered by biomedical engineers at Case Western Reserve University. Working together in Cleveland, one

of the nation's top medical hubs, provides promise for translational research.

The business community recognizes the opportunities created by Case Western Reserve University, its medical institution partners and others. Since 2001, approximately \$2.3 billion has been invested in more than 400 biomedical start-up companies in Cleveland, according to The Medical Capital initiative.

"Cleveland, The Medical Capital, is a hotbed of global health innovation," says Annette Ballou, vice president of strategic marketing and communications for BioEnterprise, which helps nurture and grow local bioscience companies. "Cleveland is an asset-rich environment that fosters collaboration, and with that comes access. Access to resources, research, funding, relationships, talent — all the things a company needs to innovate, grow and thrive."

This, in turn, attracts the attention of investors locally and worldwide.

According to The Medical Capital initiative, there were 38 Cleveland-area biomedical investors and 96 national and international investors in local companies in 2017. When all these players come together — private and public investors, biomedical companies, and clinical and research institutions — they create a rich environment for furthering ground-breaking ideas. And Case Western Reserve's biomedical engineering department is integral to many innovations.

"The biomedical engineering department plays a critical role in the success of The Medical Capital," says Ballou. "The research, innovation and talent that it creates helps fuel the biomedical sector pipeline, contributing to the growth of the region's biomedical ecosystem."

Velcheti sums it up best, saying, "There's opportunity for great things to happen here in Cleveland."

"Cleveland is often underappreciated in terms of how much of a powerhouse it is for biomedical research."

— Vamsidhar Velcheti

CLEVELAND'S IMPACT ON THE BIOMEDICAL MARKET

700+
biomedical
companies

\$2.3 billion
growth capital
since 2001

59%
growth in the regional
bioscience industry

96
national investors

38 Cleveland-area
biomedical investors

>65
acquisitions
since 2001

Statistics provided by

the Medical Capital
CLEVELAND

INNOVATIONS

DRIVING INGENUITY AT THE INTERACTIVE COMMONS

“The Interactive Commons provides a place to understand how people work together and to take the collaborative atmosphere we have here at Case Western Reserve and expand it to partners beyond our campus.”

— Mark Griswold

The intricacies of the brain remain one of the last great mysteries of the human body, comprising an exquisite network of interconnected neurons. Cameron McIntyre, a professor of biomedical engineering at Case Western Reserve University, is using cutting-edge technologies at the university's Interactive Commons (IC) to help better understand the circuitry of the brain and ultimately benefit patients with neurologic disorders ranging from Parkinson's disease to obsessive-compulsive disorder.

“Basic science has been working for a long time to create the human connectome — basically a circuitry map of the human brain,” says McIntyre, whose lab focuses on deep brain stimulation (DBS) to treat neurologic disorders. “If we know what the maps are and we know what circuits in a given disorder are dysfunctional, then we can use that to tell us where we should implant electrodes to best treat that particular disease.”

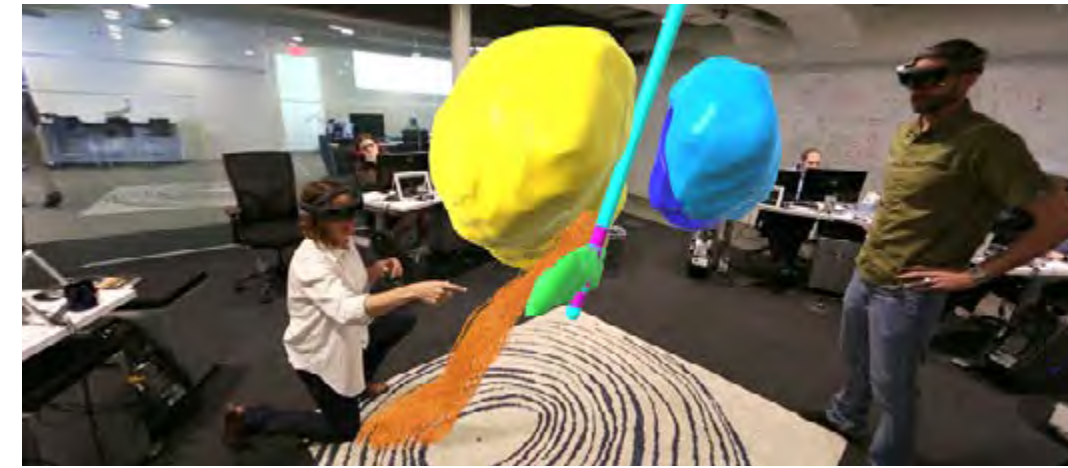
Launched in 2013, the IC fosters teamwork among disparate disciplines — from engineering to drama — to drive ingenuity in research and education. “Big advancements are going to happen at the intersections of our current disciplines,” says Mark Griswold, IC Faculty Director and a professor in the School of Medicine's

Department of Radiology. To facilitate collaboration, the IC offers several resources, such as a 24 x 8-foot “visualization wall” where users can display images from multiple computing devices simultaneously and Microsoft HoloLens, which utilizes holograms to enable people to interact naturally with digital content.

Ideally, these resources will encourage innovation through enhanced communication. “One of the biggest gaps in the multidisciplinary approach is that people get together, but can't communicate,” says Griswold. “One of the backbones of the Interactive Commons is to give people the ability to communicate through pictures and holograms — to look at their information and data in different ways.”

The Interactive Commons has a physical location — 4,500 square feet in the Thwing Building on Case Western Reserve's campus. But the boundary-breaking work done there isn't constrained by walls. Among the ongoing projects at the IC is a collaboration with faculty in the university's Department of Dance to help create educational tools for the College of Arts and Sciences in undergraduate physics.

McIntyre is just one of several faculty members in the biomedical engineering department who are



Cameron McIntyre studies neural anatomy in mixed reality using Microsoft HoloLens.



taking advantage of the IC for work on digital imaging, neuromimetic interfaces and more. McIntyre's team, which recently applied for an R01 grant from the National Institutes of Health, is building the infrastructure for a visualization environment specifically for deep brain stimulation. He partners with Griswold, other engineers and medical clinicians on the project.

“The HoloLens provides a different way to think about connections in the brain,” says McIntyre. “You can see more of a volume-based visualization as opposed to a 2-D computer screen. And you can

see how things wrap around each other in ways that are hard to do on computer screens.”

McIntyre hopes the tools his team creates can be used by neurosurgeons specializing in DBS to train fellows and residents in a holographic environment rather than in the operating room as they currently do. Neurologists could also use the technology to help program implanted devices to achieve certain therapeutic effects. “I can see how the IC, and the HoloLens in particular, will offer a completely different way of interfacing with data and a much

better way to do a lot of things we currently do with less interactive computers,” says McIntyre.

As the IC builds momentum and users, Griswold says the possibilities are endless. “The Interactive Commons provides a place to understand how people work together and to take the collaborative atmosphere we have here at Case Western Reserve and expand it to partners beyond our campus,” he says. “We have an opportunity as a university to change the way we teach and research for the better.”

Learn more about the IC at case.edu/ic

FACULTY FOCUS

Q&A WITH ZHENG-RONG LU



Zheng-Rong Lu, who joined Case Western Reserve University in 2009, is the M. Frank Rudy and Margaret Domiter Rudy Professor of Biomedical Engineering and heads the Case Center for Biomolecular Engineering. Cutting-edge research conducted by Lu's group was highlighted in two journals last spring — the June 16 issue of *Molecular Therapy – Nucleic Acids* and the April issue of *Bioconjugate Chemistry*.

What is the primary focus of your research in the Case Center for Biomolecular Engineering?

I am a chemist by training, so most of my work is associated with biomolecules. We design biomolecules for disease diagnosis and therapy, depending on the application.

Can you describe the gene delivery system you designed that is the focus of the article in *Molecular Therapy – Nucleic Acids*?

Gene delivery is still a big challenge for gene therapy, which has been around for over a half century. If somebody has a genetic disorder or disease, we can introduce a normal gene to replace the abnormal gene. Then we have a chance to cure the disease. The problem is how to deliver a normal gene into the right place – the right cells – and also not cause any unintended problems.

Most people use viruses, which work very well but have many other issues, including safety. We are trying to do something different. We've developed some simple,

smart biomolecules that can help to deliver genes into the right places. In the research featured in *Molecular Therapy – Nucleic Acids*, we tried to deliver genes to the eyes to cure some monogenic eye disorders. We showed the therapeutic efficacy of the system in a mouse model in this study. It seems safe and won't cause some of the other problems of viral systems.

What's the next step for that project?

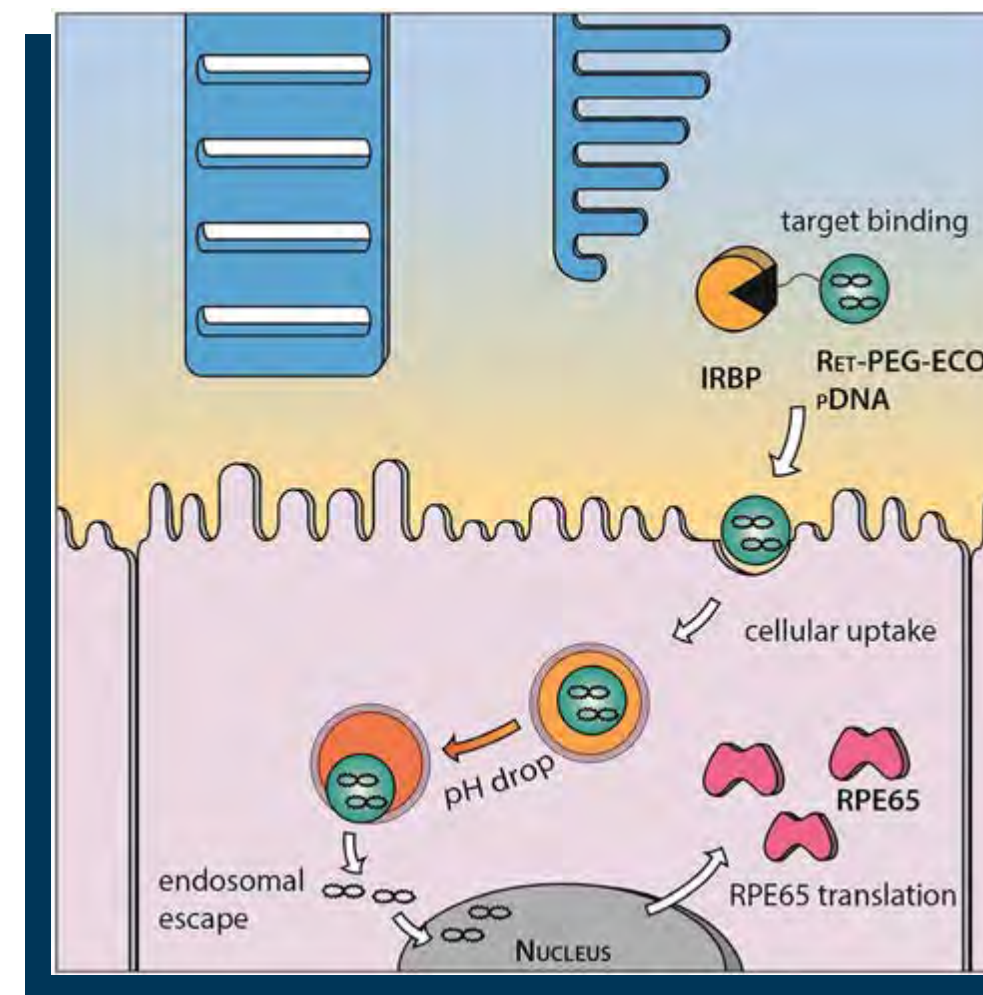
Ideally, we will move forward with clinical translation. We have a patent filed and are trying to obtain funding for translational development. Also, we'd like to extend this technology to treat some other genetic disorders in the eyes, like Stargardt disease. So the application is really broad. If we can make a breakthrough in one disorder with the system, it will have the potential to be useful for many other related diseases.

Can you talk about your research on a system to non-invasively

identify prostate tumors harboring cancer cells that's highlighted in *Bioconjugate Chemistry*?

In clinical cancer management, one big challenge is to detect cancer at an earlier stage. Then, once it's detected, doctors want to know whether the cancer is malignant — whether it has the potential to metastasize to some other part of the body — or benign. Biopsy is still the most used method today to differentiate between malignant and benign tumors, but it's not very accurate. If you don't sample in the right location, you may get wrong information.

There's a huge clinical need for something simple and non-invasive to detect cancer at a very early stage and also to differentiate aggressive tumors from benign ones. We try to approach this based on our understanding of cancer biology. We've identified a marker associated with tumor metastasis and drug resistance. We have developed a probe so we can image that protein. The probe is able to detect and identify aggressive



Modified ECO nanoparticles bind to interphotoreceptor retinoid-binding protein (IRBP), which transports them to the target cells in the retinal pigment epithelium (RPE.) The ECO is taken up by the cell through endocytosis, but the nanoparticles escape endosomes and release the RPE65 DNA into the nucleus. The RPE65 gene is then expressed by the RPE cells, protecting the photoreceptor cells and preserving vision.

CREDIT: Zheng-Rong Lu

tumors based on expression levels of the protein, which relates to the tumor aggressiveness. We've demonstrated the concept and validated the feasibility. It shows great promise.

And wouldn't knowing how aggressive a tumor is aid clinicians tremendously in deciding treatment options?

Absolutely! That's the key in cancer management and tailoring precision therapy for better treatment outcome. It is the advantage of the technology that we are working on. We have designed this technology based on our understanding of cancer biology of the biomarker, which shows strong clinical relevance. We have started the

FDA-required safety evaluations and hope to start a clinical trial soon.

Ultimately, what are the translational benefits of your work on differentiating the aggressiveness of tumors?

Once cancer is diagnosed, it's often treated aggressively — even some of the cancers that aren't life-threatening. The problem is we can't accurately differentiate the aggressiveness of tumors, so everybody is treated aggressively. If you can differentiate aggressiveness, doctors will design different approaches to treat different types of cancers. This may eliminate unnecessary procedures and spare a large number of

patients from invasive procedures, thereby reducing the cost of healthcare.

Multidisciplinary work is key to advancing these kinds of solutions. What cross-disciplinary partnerships do you have?

I have several collaborations across the campus and in the local medical community. We collaborate with other biomedical engineers in the Case School of Engineering, as well as basic scientists in the School of Medicine and in the Case Comprehensive Cancer Center. We also collaborate with physicians from University Hospitals and Cleveland Clinic. Without these partnerships, it would be very hard to do the things we're doing now.

OUR PEOPLE MAKING AN IMPACT

PHD SPOTLIGHT



Erika Cyphert

Erika Cyphert, a graduate research assistant in the Center for Delivery of Molecules and Cells, has received two fellowships: an American Heart Association Predoctoral Fellowship and a National Science Foundation Graduate Fellowship. Cyphert works under the tutelage of Horst von Recum, professor of biomedical engineering and principal investigator in the Center for Delivery of Molecules and Cells, which focuses on creating polymers for drug delivery for a wide range of diseases.



Prateek Prasanna

Prateek Prasanna was among a team of researchers who won first-place in the collegiate division of the inaugural Medical Capital Innovation Competition earlier this year for development of NeuroRadVision imaging software that distinguishes between a recurrent brain tumor and benign effects of radiation. The team was led by Pallavi Tiwari, assistant professor of biomedical engineering and director of the Brain Image Computing (BrIC) Laboratory. Prasanna also earned the 2017 Doctoral Excellence Award from the School of Medicine at Case Western Reserve University.

ALUMNI HIGHLIGHTS



William Timmons

William D. Timmons (GRS '92), launched Elastance Imaging LLC, a medical device startup company that injects low frequency (audio) tactile shear waves into tissue as a contrast agent to estimate mechanical properties. Using standard ultrasound, MR, CT, OCT and other imaging techniques, the company tracks the speed of sound in tissue to determine Young's modulus and viscosity on a pixel-by-pixel basis, and overlays them in real time on the regularly scanned image. Hard objects, such as tumors and fibroses, as well as soft objects like fatty infiltration, show up clearly. Timmons says the technology is cost effective and poised to save many lives. Anyone interested in learning more or becoming part of the team can contact Timmons at wtimmoms@ElastanceImaging.com or 614-579-9520.



Michael Ackermann

Michael Ackermann (GRS '09) is Vice President, Neurostimulation for Allergan plc, a global pharmaceutical company headquartered in Dublin. Formerly, he was co-founder and CEO of Oculeve Inc., which was acquired by Allergan in 2015. Oculeve created novel treatments for dry eye disease, including OD-01, a non-invasive nasal neurostimulation device that increases tear production in patients with dry eye disease.



Jaeyon Kim

Jaeyon Kim (GRS '08) was named Associate Director of Pharmacometrics at Novartis in Cambridge, Mass. Prior to joining Novartis, Kim worked for Merrimack Pharmaceuticals for nearly 10 years, most recently as Associate Director of Quantitative Clinical Pharmacology and Pharmacometrics.



EMINENT ALUMNI CHECKING IN WITH ERIC PERREAULT

Eric Perreault (GRS '00) is chair of the Department of Biomedical Engineering at the McCormick School of Engineering and Applied Science at Northwestern University, a professor of physical medicine and rehabilitation, and a research scientist at the Shirley Ryan AbilityLab. Before relocating to the Windy City, Perreault spent four years in Cleveland as a graduate student in Case Western Reserve University's Department of Biomedical Engineering.

What are the strengths of the graduate program in biomedical engineering at Case Western Reserve University?

There are many strengths. It is one of the founding departments in biomedical engineering and has a long history of great research and education. That's what attracted me as a student. The university's research programs, particularly those aligned with my interests in human movement control and neuroprosthetics, are fantastic. I also had some phenomenal teachers. I still remember lectures with Tom Mortimer, Dominique Durand and many other faculty members. As a student, they fueled my growing interest about the field of biomedical engineering.

Are there any memories of your time at CWRU that stand out?

The primary thing I remember is the faculty – particularly my two mentors, Bob Kirsch and Pat Crago. They not only supported my scientific growth, but took great care to promote my professional development. I learned much about how universities work and how to excel as a scientist in an academic setting. From the day I walked onto campus, they treated me like a colleague rather than a student. From them, I was given so many opportunities that have contributed to where I am today.

Speaking of those contributions, how did being a graduate student at Case Western Reserve prepare you for a career as a professor and researcher?

There are countless ways. One of the things I observed at Case Western

Reserve for the first time as a young scientist was this idea of working with clinicians and doing patient-centered research. My work was, and still is, focused more on the basic rather than applied end of things. But many of our projects are driven by conversations I have with clinicians – identifying physiological mechanisms or other scientific and engineering questions that are relevant to clinical care. A close collaboration between clinicians and scientists is one of the things I was exposed to at Case and MetroHealth Medical Center, where the lab I worked in was embedded. It is also the model for research at the Shirley Ryan AbilityLab, where my current research group now resides.

And has anything from your time at Case Western Reserve helped in your role as chair of the Department of Biomedical Engineering at Northwestern?

Northwestern's Department of Biomedical Engineering has a long-standing and pervasive culture of collaboration and translation. I think that I was well-prepared to walk into this position in part because of the collaborative environment I experienced at Case Western Reserve. I am admittedly biased, but I consider my current department to be a model of collegiality and excellence, working together to support the success of all research groups and linking that success back to the growth of the entire department. I observed a similar spirit in the Cleveland FES Center [of which CWRU is a consortium partner] and brought some of the spirit with me to Northwestern.

Under your leadership, what accomplishments have been achieved at Northwestern?

Biomedical engineering at Northwestern has been in a tremendous period of growth. We have hired seven tenured or tenure-track faculty since I became chair two years ago. This has given me a great opportunity to think about the future of biomedical engineering here at Northwestern and more broadly. Working with our faculty, I have been assessing our core strengths and looking at new areas for opportunity. We have been able to hire a stellar group of junior and senior faculty who build on our strengths, while also helping us branch into exciting new directions. I am personally interested in new directions that link our traditional areas of expertise, such as biomaterials and neural engineering, through transformative engineering technologies. I think we have done a good job exploiting those opportunities.

Chicago is revered as a destination city. What do you tell people in the Windy City about Cleveland, which doesn't get nearly as much attention?

I tell them it's great! The first thing I noticed about Cleveland is without a doubt the people, who are just spectacular. I love the frankness and good company of the many friends and colleagues I met in Cleveland — and subsequently in Chicago. The two cities share this most important of resources.



CHECK OUT DEPARTMENT RESEARCH VIDEOS

The department's research overview videos showcase current high-potential projects underway in the labs.

View all of the new videos on our YouTube channel.



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