IN PURSUIT OF A WHOLE BLOOD SUBSTITUTE

CWRU researchers play an instrumental role in $46.4 million DARPA project to develop biosynthetic whole blood.

FULL STORY, p. 12

CASE WESTERN RESERVE UNIVERSITY | *Biomedical Engineering Alliance* | Cleveland Clinic

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The Biomedical Engineering Alliance
at Case Western Reserve University and Cleveland Clinic

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The spring 2024 newsletter has been created by the BME Alliance Publicity Committee.

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FROM THE CHAIRS

One of the strengths of the Biomedical Engineering Alliance between Case Western Reserve University and Cleveland Clinic is that our staff members are involved in an array of core areas, from artificial intelligence to neural engineering and rehabilitation. This diversity creates an environment where our 60-plus primary faculty – and dozens more associated and research faculty – find synergies among their work and push one another to view projects from a different lens.

Feature articles in this issue of our newsletter highlight research projects and collaborations in three of our research thrusts – biomaterials, immunoengineering and biomedical imaging.

Biomaterials – Anirban Sen Gupta, the Wallace R. Persons Endowed Professor of Engineering at Case Western Reserve University, is an investigator on an ambitious four-year, $46.4 million project funded by the Defense Advanced Research Projects Agency to develop a bioartificial whole blood surrogate. The potential for use in surgeries, injuries, disease and bleeding disorders is immeasurable.

Immunoengineering – Newly-appointed Assistant Professor Abhinav Acharya's research is at the intersection of biomaterials and immunoengineering. His lab is designing biomaterials to modify the metabolism of immune cells and see if it affects disease outcome. Ultimately, that could lead to translatable products to treat inflammatory conditions, autoimmune diseases, cancer and other conditions.

Biomedical Imaging – Cleveland Clinic is planning two new cutting-edge medical imaging centers. As part of a strategic partnership, the healthcare system and Canon Inc. expect to establish a comprehensive imaging research center where cross-institutional teams will focus on projects in cardiology, neurology and musculoskeletal medicine. In addition, the Arthritis Foundation designated Cleveland Clinic as the future home for its Osteoarthritis Imaging Center.

With so much going on within the Biomedical Engineering Alliance, it's challenging for us to narrow down a handful of projects and partnerships to focus on in feature articles. You can get a glimpse of the extent of our work in the Faculty & Staff Highlights, which include news about grants, journal publications, awards and more from biomedical engineering staff at Case Western Reserve University and the Cleveland Clinic Lerner Research Institute.

We're also proud to teach and mentor the next generation of biomedical engineers. The Student Spotlight gives well-deserved attention to undergraduate and graduate students who have earned research awards, landed highly sought after fellowships and won paper and poster awards. One of our PhD candidates at Case Western Reserve University, Leah Roldan, was honored to meet President Biden last fall and share details about her work at the Advanced Platform Technology Center and Human Fusions Institute on neural interfaces for prosthesis sensory feedback.

There is a lot going on in Cleveland, and we're excited to share it with you. We'd also love to hear from you. If you have a comment about one of our stories or you're among our alumni and want to share news, reach out to us at bme-news@case.edu.

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STUDENT SPOTLIGHT

PhD Candidate Earns Award from Parkinson's Foundation

Prajakta Joshi

Prajakta Joshi, a doctoral candidate in biomedical engineering at Case Western Reserve University, received the Visiting Researcher Award from the Parkinson's Foundation. The award, which includes a $4,000 stipend, facilitated Joshi's journey to work with Dr. Sanjay Pandey, head of the Department of Neurology at Amrita Hospital, Faridabad, India. Working alongside Dr. Pandey, Joshi gained experience conducting intraoperative microelectrode recordings of the subthalamic nucleus in response to external stimuli-like vibration. Neural recordings offer immense potential for identifying aberrant brain processes that underlie intricate disease states.

Doctoral Candidate Lands on 30 Under 30 List

Palak Gupta

Palak Gupta, a biomedical engineering graduate student at Case Western Reserve University, was named to Forbes' 30 Under 30 Cleveland Local list. She was recognized for her research on understanding the effects of electrical stimulation on visuospatial navigation and visuomotor deficits in movement disorders, primarily Parkinson's disease.

Two Students Awarded Fellowships

William Wulftange

William Wulftange, an MD/PhD candidate in the CWRU School of Medicine, earned a predoctoral fellowship from the American Heart Association. Wulftange, who is pursuing a doctorate degree in biomedical engineering, works in the lab of Umut Gurkan, Wilbert J. Austin Professor of Engineering, where he is investigating CAR-T cell interactions with the blood-brain barrier.

Zoe Sekyonda

Zoe Sekyonda, a PhD candidate who also works in Gurkan's lab, received two awards. She earned the American Society of Hematology Graduate Hematology Award and Fellowship, as well as the National Institute of Biomedical Imaging and Bioengineering (NIBIB) new RADx® Tech DIVE fellowship. The NIBIB fellowship helps underrepresented biotechnology innovators advance their products. Sekyonda built a device that quickly measures oxygen levels in blood samples.

Scholar-Athlete Honored

Aniya Hartzler, an undergraduate biomedical engineering student at Case, was named to the United Soccer Coaches' Scholar All-America First Team. She is the first player in the university's women's soccer program to earn first-team honors. Hartzler was a pivotal member of the Spartan backline, helping the defense record nine shutouts and allow just 10 goals during the 2023 season.

Papers and Posters Win Awards

Four students in the Department of Biomedical Engineering at Case Western Reserve University won awards at conferences. Victoria Laney, a graduate student, won a poster award in the oncology category and the Science Slam Award for her presentation, "MRI Molecular Imaging of anti-VISTA mAb Therapy in Pancreatic Cancer" at the World Molecular Imaging Society 2023. Ved Shivade, a third-year undergraduate, won Best Paper of Session at the 2023 Cornea and Eye Banking Forum for his presentation, "Donor Cornea Automatic Endothelial Cell-Density Analysis." Graduate student Kihwan Lin's abstract, "The Effect of Long-term Exercise Training on Metabolic Responses in Obese Zucker Fatty Diabetic Rats using Phosphorous-31 MRS," was selected as one of the top 100 abstracts at the International Society for Magnetic Resonance in Medicine 2023 Annual Meeting. Undergraduate student Chuba Ozor won the oral portion of the Technical Research Exhibition at the National Society for Black Engineers Region IV Conference.

Ved Shivade, center, receives award for Best Paper of Session at the 2023 Cornea and Eye Banking Forum.

Chuba Ozor, right, presents his poster at the Technical Research Exhibition at the National Society for Black Engineers Region IV Conference.

Student Shares Research with President Biden

Leah Roldan, a PhD candidate, met President Biden during the "American Possibilities: A White House Demo Day" in Washington, D.C., in November. The demo day showcases science and technology spurred by federal R&D and the president's Investing in America agenda. As a graduate student researcher at the Advanced Platform Technology Center and Human Fusions Institute, Roldan participates in Dustin Tyler (Kent H. Smith Professor II of Biomedical Engineering at Case Western Reserve University) and CWRU Assistant Professor Emily Graczyk's "Neural Interfaces for Prosthesis Sensory Feedback" study with the U.S. Department of Veterans Affairs. "It was a really cool experience to learn about other research and tech being developed and such an honor to get to explain some of our lab's work to President Biden," shared Roldan on LinkedIn.

Grad Student Wins Travel Award to NIH BRAIN Initiative Meeting

Muthumeenakshi Subramanian, a PhD candidate, won a travel award and honorarium to the National Institute of Health's 9th annual BRAIN Initiative® Meeting in June 2023. Subramanian works in the laboratory of Dominique Durand, Elmer Lincoln Lindseth Professor in Biomedical Engineering at Case Western Reserve University, where she studies the non-synaptic propagation of neural activity, such as epileptic events and theta waves. During the BRAIN Initiative Meeting, she presented a poster entitled, "Extracellular voltage clamp suppresses epileptic activity in mice hippocampus."

FACULTY & STAFF HIGHLIGHTS

Jay L. Alberts

Jay L. Alberts, staff, Lerner Research Institute Department of Biomedical Engineering, The Edward F. and Barbara A. Bell Family Endowed Chair, director of Cleveland Clinic's Concussion Center and vice chair of Innovation with Cleveland Clinic's Neurological Institute, was awarded an R01 grant from the Department of Defense for his project titled, "Identifying the Neural Signature of Exercise to Advance Treatment of Parkinson's Disease (PD) Cognitive Declines." The project aims to provide insight into the neural mechanisms underlying executive functioning changes in patients with PD, systematically measuring neural activity to understand how exercise impacts the function of the basal ganglia and its cognitive-motor network, with the potential to replicate these effects through specific deep brain stimulation parameters, offering an alternative to an "exercise pill" in the form of exercise deep brain stimulation. In addition, Alberts received an R01 grant from the National Institute of Health's (NIH) National Institute of Neurological Disorders and Stroke (NINDS), which also aims to investigate the relationship between genetics, aerobic exercise and PD patients. The combined grants total more than $1 million in federal funding in 2023.

Hamid Charkhkar

Hamid Charkhkar, a research assistant professor in the Department of Biomedical Engineering at Case Western Reserve University, received a $1.49 million grant from the U.S. Department of Defense's Congressionally Directed Medical Research Programs. As principal investigator, Charkhkar will partner with co-investigators from the Department of Biomedical Engineering and the University of Illinois Chicago, as well as clinicians from the Louis Stokes Cleveland Veterans Affairs Medical Center, to study neurally integrated lower limb prothesis for home and community use.

The project builds on earlier development of a neuroprosthesis that restores plantar sensation to individuals with lower limb loss by electrically activating the remaining nerves in the residual limb via an implanted neural interface. "In this four-year project, we aim to take the next logical step to understand the real-world benefits of this technology by investigating its effects when used freely at home and in the community during self-selected daily activities," says Charkhkar.

Margot Damaser

Margot Damaser, staff, Lerner Research Institute Department of Biomedical Engineering, was inducted into the National Academy of Inventors (NAI) as a Senior Member. The cohort of 429 Senior Members are active researchers who "foster the spirit of innovation within their communities and institutions while educating and mentoring the next generation of inventors." In addition, Damaser's article, "First in Human Subjects Testing of the UroMonitor: A Catheter-free Wireless Ambulatory Bladder Pressure Monitor," was the featured cover story in the July 2023 issue of the Journal of Urology. The UroMonitor is the first device to enable catheter-free telemetric ambulatory bladder pressure monitoring in humans and promises to help patients and physicians more reliably identify bladder events.

Kathleen Derwin

Kathleen Derwin, vice chair and associate staff, Lerner Research Institute Department of Biomedical Engineering, was selected as an Orthopaedic Research Society (ORS) Fellow of the Year (2023). Additionally, Derwin and a team of principal investigators who direct Cleveland Clinic's Musculoskeletal Research Center, were one of only three centers to be awarded an "LRI Center of Excellence in Osteoarthritis." This two-year (Phase I) grant will provide resources and establish a Musculoskeletal Biomarkers Core, a Data Science Core and launch three additional projects. The underlining goal is to build a foundation around a highly prevalent and debilitating musculoskeletal condition (osteoarthritis), from which future extramural grants and philanthropic funding can be obtained.

Dominique Durand, left, receives the 2024 Engineering Innovator Award from the North American Neuromodulation Society.

Dominique Durand

Dominique Durand, the Elmer Lincoln Lindseth Professor in Biomedical Engineering at Case Western Reserve University, won the 2024 Engineering Innovator Award from the North American Neuromodulation Society. The award recognizes his accomplishments as a world-renowned researcher in neural engineering, computational neuroscience, neurophysiology and control of epilepsy, non-linear dynamics of neural systems, neural prostheses, and applied magnetic and electrical field interactions with neural tissue. Durand has published more than 160 peer-reviewed articles, serves on 14 editorial boards of peer-reviewed scientific journals and has consulted for many biotechnology companies and foundations.

Ahmet Erdemir

Ahmet Erdemir, associate staff, Lerner Research Institute Department of Biomedical Engineering and director at the Computational Biomodeling (CoBi) Core, serves as one of Cleveland Clinic's lead investigators for the Discovery Accelerator "Digital Technologies and Artificial Intelligence" project. This innovative partnership between Cleveland Clinic and IBM resulted in the unveiling of the first quantum computer dedicated to healthcare research, deployed at Cleveland Clinic's main campus. In addition, Erdemir was awarded a four-year $2.3 million R01 grant from the National Institute of Health (NIH), National Institute of Biomedical Imaging and Bioengineering (NIBIB) for his proposal, "Reproducibility in simulation-based prediction of natural knee mechanics." Five teams led by knee biomechanics experts are developing knee computational models to analyze current practices in joint and tissue mechanics, with the goal of establishing reliable knee joint models for simulation-based discoveries and medical device design and evaluation.

David Escobar

David Escobar, assistant staff, Lerner Research Institute Department of Biomedical Engineering and director of Cleveland Clinic's Neural Dynamics and Modulation Laboratory, was awarded a five-year R01 grant from the National Institute of Health (NIH), National Institute of Neurological Disorders and Stroke (NINDS). This $3 million award will support Escobar's research to identify the specific neural dynamics that underlie movement disruption in patients with Parkinson's Disease (PD). Escobar's proposal will leverage insights into neural circuits to further advance deep brain stimulation (DBS) technologies.

Agata Exner

Agata Exner was appointed director of Case Western Reserve University's Center for Imaging Research. The globally acclaimed expert in molecular imaging and theranostics also serves as the Henry Willson Payne Professor and vice chair of basic research in the university's Department of Radiology, as well as professor in the Department of Biomedical Engineering.

Chris Flask

Chris Flask, professor of radiology, biomedical engineering and pediatrics in the CWRU School of Medicine, was one of 59 investigators to receive the 2023 Distinguished Investigator Award from the Academy for Radiology & Biomedical Imaging Research. In November, he was inducted into the Academy's Council of Distinguished Investigators during the annual meeting of the Radiological Society of North America. In addition, Flask's groundbreaking research in MRI and imaging technology was featured recently in a Bruker BioSpin Customer Insight article entitled, "Imaging Serves as a Scientific Hub to Unite Preclinical and Clinical Research."

Kiyotaka Fukamachi

Kiyotaka Fukamachi, staff, Lerner Research Institute Department of Biomedical Engineering, and Taiyo Kuroda, a postdoctoral research fellow in his lab, were selected as Cleveland Clinic Catalyst SPARK Award recipients for the project titled, "Freedom from driveline for LVAD patients: Abdominal Implantable Battery and trans-umbilicus energy transmission system." Fukamachi's lab aims to create a wireless charging battery system, designed to be implanted into the abdominal region, with the goal of providing power to a left ventricular assist device (LVAD) without the need for skin-penetrating cables.

Chaitali Ghosh

Chaitali Ghosh, staff scientist, Lerner Research Institute Department of Biomedical Engineering, was selected to be a Fellow of the American Epilepsy Society (FAES). This designation honors researchers who have demonstrated long-term dedication and commitment to advance both the AES mission and the field of epilepsy. Ghosh was invited to present her research, "GLUT1 and Cerebral Glucose Hypometabolism Signatures in Human Focal Cortical Dysplasia Linked to Hypermethylation of Key Glucose Regulatory Targets," at both the AES and the International League Against Epilepsy (ILAE) annual meetings as a featured speaker.

Vijay Krishna

Vijay Krishna, associate staff, Lerner Research Institute Department of Biomedical Engineering, was one of 12 researchers globally to receive the Wellcome Leap Foundation's "Quantum for Bio Challenge" (Q4Bio) award. The global challenge focuses on expediting the research and development of quantum computing applications in healthcare. The award will fund Krishna's proposal, "Quantum Computing for Photon-Drug Interactions," a multi-site, multi-disciplinary, collaborative endeavor between Cleveland Clinic, IBM Quantum and Algorithmiq. Krishna, one of the three co-principal investigators managing the project, and his team will receive funding of $4.25 million over three years.

Vinod Labhasetwar

Vinod Labhasetwar, staff, Lerner Research Institute Department of Biomedical Engineering, was awarded a Cleveland Clinic Catalyst SPARK Award to fund research to develop nanoparticle-delivered treatments for stroke and other clotting diseases. Labhasetwar also published the article, "Nanotechnology in Stroke: New Trails with Smaller Scales," in the journal Biomedicines. Labhasetwar's lab strives to address the need for effective stroke treatment, as current FDA-approved interventions – such as tissue plasminogen activator (tPA) and endovascular thrombectomy (EVT) – are limited by a short therapeutic time window and potential adverse effects. The lab aims to develop nanoparticle-based approaches that lead to safer, multifunctional thrombolytic agents, with the potential to improve clinical outcomes in stroke patients.

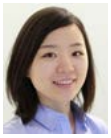
Shuo Li

Shuo Li, associate professor in the Department of Biomedical Engineering at Case Western Reserve University, is part of a team that received a $1.1 million grant from the National Science Foundation. Li and colleagues from the Case School of Engineering, CWRU School of Medicine, CWRU Center for Imaging Research and the University Hospitals Cleveland Medical Center are developing a virtual contrast-enhanced imaging technique as an alternative to medical imaging processes that use chemical contrast agents. Li and other members of the CWRU Center for Imaging Research also received the Best Paper Award – Runner Up at the 2023 International Conference on Medical Image Computing and Computer Assisted Intervention for their paper, "Spatiotemporal knowledge teacher-student reinforcement learning to detect liver tumors without contrast agents."

Xiaojuan Li

Xiaojuan Li, staff, Lerner Research Institute Department of Biomedical Engineering and director of the Program for Advanced Musculoskeletal Imaging (PAMI), and her lab were selected as recipients of The Journal of Orthopaedic Research (JOR) "Excellence in Basic Science Award" for their article, "Shear strain and inflammation-induced fixed charge density loss in the knee joint cartilage following ACL injury and reconstruction: A

computational study." The study demonstrates that excessive tissue deformation and acute inflammation after ACL injury and reconstruction surgery hasten fixed charged density (FCD) loss and cartilage degeneration, where biomechanical and biochemical models predict FCD loss, showing localized FCD loss near the lesion, and simulated reduction of cytokine concentration leads to partial FCD content recovery, highlighting the potential for estimating in vivo FCD loss post-injury and aiding post-traumatic osteoarthritis (PTOA) progression prediction and treatment interventions.



Dan Ma

Dan Ma, assistant professor in the Department of Biomedical Engineering at Case Western Reserve University, is co-principal investigator on a $3.05 million grant from the National Institutes of Health and National Cancer Institute to study whether magnetic resonance fingerprinting (MRF) can predict early response to neoadjuvant chemotherapy in patients with breast cancer. MRF is a novel approach to MRI that allows multiple tissues in the body to be examined by taking a single image, or "fingerprint." Ma is leading the study with Holly Marshall, associate professor in the School of Medicine and division chief of breast imaging at University Hospitals, and Yong Chen, assistant professor of radiology at the School of Medicine.

In addition, Ma and Chaitra Badve, associate professor in the Department of Radiology at the School of Medicine, presented a poster entitled, "Motion robust MR fingerprinting scans for non-sedated infant imaging" at the International Society for Magnetic Resonance in Medicine's 2023 annual meeting. Ma was also named to Crain's Cleveland Business 2023 40 Under 40 list, which recognizes the best and brightest professionals in northeast Ohio.

Christopher Nguyen

Christopher Nguyen, director of the Cardiovascular Innovation Research Center; director of MRI research in the Sydell and Arnold Miller Family Heart, Vascular & Thoracic Institute at Cleveland Clinic; and associate staff, Lerner Research Institute Department of Biomedical Engineering, was featured in Nature magazine in December 2023. The report highlighted a ground-breaking achievement in the field of cardiac medicine: a successful robotic replica of the heart's right chamber. This collaborative effort with scientists from the Massachusetts Institute of Technology (MIT), Massachusetts General Hospital and Boston Children's Hospital unveiled the bio-robotic model, which simulates the function of the heart's right ventricle, mimicking its real pumping action. The model could help to evaluate new implants and devices to treat an array of cardiac disorders. This was Nguyen's second appearance in Nature in 2023. Earlier in the year, his article, "An implantable soft robotic sleeve for the recapitulation of aortic stenosis," was the featured cover story of the October Nature Biomedical Engineering issue.

Ela Plow

Ela Plow, associate staff, Lerner Research Institute Department of Biomedical Engineering, received a two-year Department of Defense U.S. Army Medical Research and Development Command, Congressionally Directed Medical Research Programs (CDRMP), Spinal Cord Injury Program (SCRIP) Investigator-Initiated Research Award (IIRA) for her proposal, "Biomarkers of Response to Neurorestorative Therapies in Cervical SCI." The grant will fund research to test the hypothesis that transcranial, direct-current stimulation (tDCS), when combined with rehabilitation, has positive effects on upper-extremity (UE) motor outcomes in chronic tetraplegia in association with improved corticomotor physiology.

Anirban Sen Gupta

Anirban Sen Gupta, the Wallace R. Persons Professor in the Case School of Engineering, was named a Fellow of Biomaterials Science and Engineering (FBSE), the highest honor among the global biomaterials community. The fellowship, presented by the International Union of Societies for Biomaterials Science and Engineering, recognizes the innovative work conducted in Sen Gupta's lab, including development of synthetic platelets to treat hemorrhagic complications and inherited blood disorders, as well as integration of such technologies to create biosynthetic whole blood.

"It is also an opportunity for me to work with my peers in the global biomaterials community to advocate for education and research in our field and enhance the impact on global healthcare, recognizing the opportunities, challenges and disparities that exist across the world in this area," says Sen Gupta.

Ron Triolo

Under the leadership of Executive Director Ron Triolo, the Advanced Platform Technology Center was renewed through the end of the decade as a Department of Veterans Affairs Research Center in the Rehabilitation Research and Development Service. The APT Center addresses the clinical needs of disabled veterans through the development, clinical translation and dissemination of novel rehabilitation devices and interventions. "This renewal would not have been possible without the hard work and dedication of the team at the APT Center to improve the lives of veterans each and every day," says Triolo, who is also a professor in the Department of Biomedical Engineering at Case Western Reserve University.

Triolo also secured a $1.2 million, four-year Rehabilitation Research and Development Merit Award from the Department of Veterans Affairs for the study, "Neural Stimulation to Enhance Community Mobility After Incomplete SCI." The goal of the project is to enable veterans with partial paralysis to improve their daily walking capabilities through development of practical and readily customizable control systems for peripheral nerve stimulation to augment the actions of selected muscles based on real-time feedback of voluntary body movements.

Satish Viswanath

Satish Viswanath, associate professor in the Department of Biomedical Engineering at Case Western Reserve University, received the 2023 Imaging Informatics Innovator Award from the Society for Imaging Informatics in Medicine. He also was named to Crain's Cleveland Business 2023 Notables in Education Leadership list.

In addition, Viswanath traveled to Malaysia in August as part of the U.S. Department of State's Fulbright Specialist Program, where his work centered on artificial intelligence (AI) and digital pathology – two areas closely aligned with his lab's focus at Case. The INVent Lab develops AI schemes to enable precision medicine by unlocking embedded information captured by different modalities in an intuitive way. In October, the INVent Lab was issued a patent on structural rectal atlas deformation features for characterizing intra-wall and peri-wall chemoradiation response on MRI.

David Wilson

David Wilson, the Robert Herbold Professor of Biomedical Engineering at Case Western Reserve University, and Sanjay Rajagopalan, chief of cardiovascular medicine for University Hospitals (UH) Cleveland Medical Center and director of the Case Cardiovascular Research Institute at Case Western Reserve University School of Medicine, are co-principal investigators on two grants from the National Institutes of Health to predict cardiovascular disease through artificial intelligence techniques.

The funding, totaling $6.2 million, is based on the CLARIFY Registry, a UH initiative offering free CT scan calcium score assessments to community members with high-risk factors for heart disease. The study will employ cutting-edge AI technologies using machine- and deep-learning models to recognize complex patterns in medical images and usher in a new era of predictive health analytics to automate risk assessment.

Mei Zhang

Mei Zhang, assistant professor in the Department of Biomedical Engineering at Case Western Reserve University and a member of the Case Comprehensive Cancer Center's Immune Oncology Program, has been awarded $2.2 million from the Department of Defense. The three-year award will fund research to develop an innovative adjuvant therapy designed to transform tumor-associated inflammation into tumor-reactive immune responses by focusing on the differentiation epitopes in CD11b, crucial markers on tumor-associated inflammatory monocytes. Zhang's research has been featured in several scientific journals, including a June 2023 article in the Journal for ImmunoTherapy of Cancer with an impact factor of 12.43. The innate immune cell engager developed by Zhang's team received FDA approval for orphan drug and rare disease designations in 2020.

BME Faculty Land University Awards

Several biomedical engineering faculty members earned awards from Case Western Reserve University in 2023, including the following:

Faculty Distinguished Research Award

Robert Kirsch, Allen H. and Constance T. Ford Professor and chair of the Department of Biomedical Engineering

Umut Gurkan, Wilbert J. Austin Professor of Engineering, Department of Mechanical and Aerospace Engineering and Department of Biomedical Engineering

Commercialization Award

These faculty had a newly-licensed technology through the university's Technology Transfer Office:

Emily Graczyk, assistant professor

Mark Griswold, professor

Kenneth Gustafson, associate professor

Michael Jenkins, associate professor

Michael Moffitt, associate professor

Dustin Tyler, Kent H. Smith Professor II of Biomedical Engineering

Inventor Award

These faculty received at least one issued patent through the university's Technology Transfer Office:

Dominique Durand, Elmer Lincoln Lindseth Professor in Biomedical Engineering

Mark Griswold, professor

Zheng-Rong Lu, professor

Grant McCallum, research assistant professor

Debra McGivney, assistant professor

P. Hunter Peckham, professor emeritus

Anirban Sen Gupta, Wallace R. Persons Professor of Engineering

Ronald Triolo, professor

Dustin Tyler, Kent H. Smith Professor II of Biomedical Engineering

Matthew Williams, assistant professor

David Wilson, Robert J. Herbold Professor of Biomedical Engineering

Xin Yu, F. Alex Nason Professor II of Biomedical Engineering

IN THE NEWS

ideastream public media

CWRU researchers ready to test device that could restore sense of feeling for mastectomy patients

A team of Case Western Reserve University engineers, led by Emily Graczyk, assistant professor in the Department of Biomedical Engineering, and Dustin Tyler, Kent H. Smith Professor II of Biomedical Engineering, are collaborating with engineers from the University of Chicago to test an implantable device that could restore the sense of feeling to breast cancer patients who have had reconstructive surgery.

FOX 8 WJW-CLEVELAND

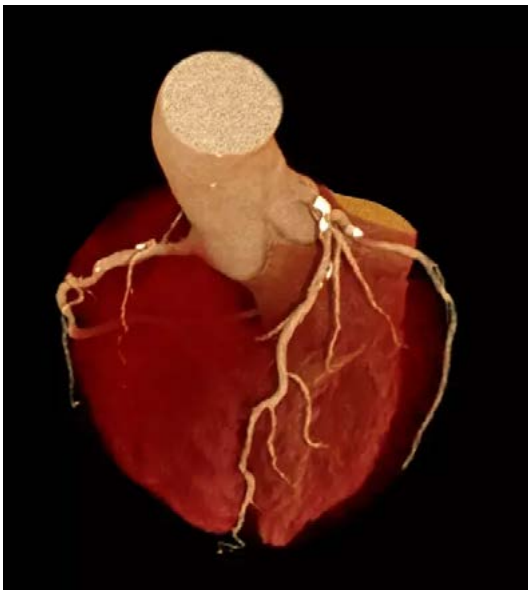
Ground-breaking Imaging Research

Fox 8 Cleveland: Dan Ma, assistant professor of biomedical engineering; Mark Griswold, the Pavey Family Designated Professor of Innovative Imaging-Revolutionizing the Worlds of Education; Chris Flask, professor of radiology, shared their work alongside physicians and scientists from University Hospitals developing a transformative magnetic resonance fingerprinting technology that was recently approved by the FDA.

Cleveland Clinic

New Centers to Advance Imaging Innovations

Cleveland Clinic set to open two imaging centers with industry and foundation partners



Courtesy of Marcus Chen, National Institutes of Health.

Cleveland Clinic has been a trailblazer in magnetic resonance imaging technology for more than four decades, opening the first building designed to house MRI machines – the Meyer Center for Magnetic Resonance Imaging – in 1983. The academic medical center further advanced its leadership in the field last fall with the announcement of two cutting-edge medical imaging centers – an imaging research center in partnership with Canon Inc. and the Osteoarthritis Imaging Center in collaboration with the Arthritis Foundation.

Creating Technologies that Transform Patient Care

Cleveland Clinic and Canon will form a strategic research partnership to develop innovative imaging and healthcare IT technologies aimed at improving diagnosis, care and outcomes for patients. The two organizations expect to establish a comprehensive imaging research center that brings together a cross-institutional team of clinician scientists, researchers and engineers. Joint research projects will focus on cardiology, neurology and musculoskeletal medicine and will have three primary components – preclinical imaging, human imaging and image analysis.

"There are so many synergies that we have between the two institutions," said Geoff Vince, Cleveland Clinic's executive director of Global Innovations and chair of the Lerner Research Institute Biomedical Engineering Department, during an announcement of

Leaders from Cleveland Clinic and Canon announced the partnership Nov. 27, 2024.

the partnership at the Radiological Society of North America's 2023 Annual Meeting in November. "When you see what Canon has achieved and what Cleveland Clinic has done over the past 100 years, the synergy is just natural. I think what is even more exciting is what we can do together in the future."

The center will be part of the Cleveland Innovation District, a $500 million-plus private-public partnership between the state of Ohio, JobsOhio (the state's private economic development corporation) and Cleveland's healthcare and higher education institutions to accelerate research, create jobs and educate the workforce of the future.

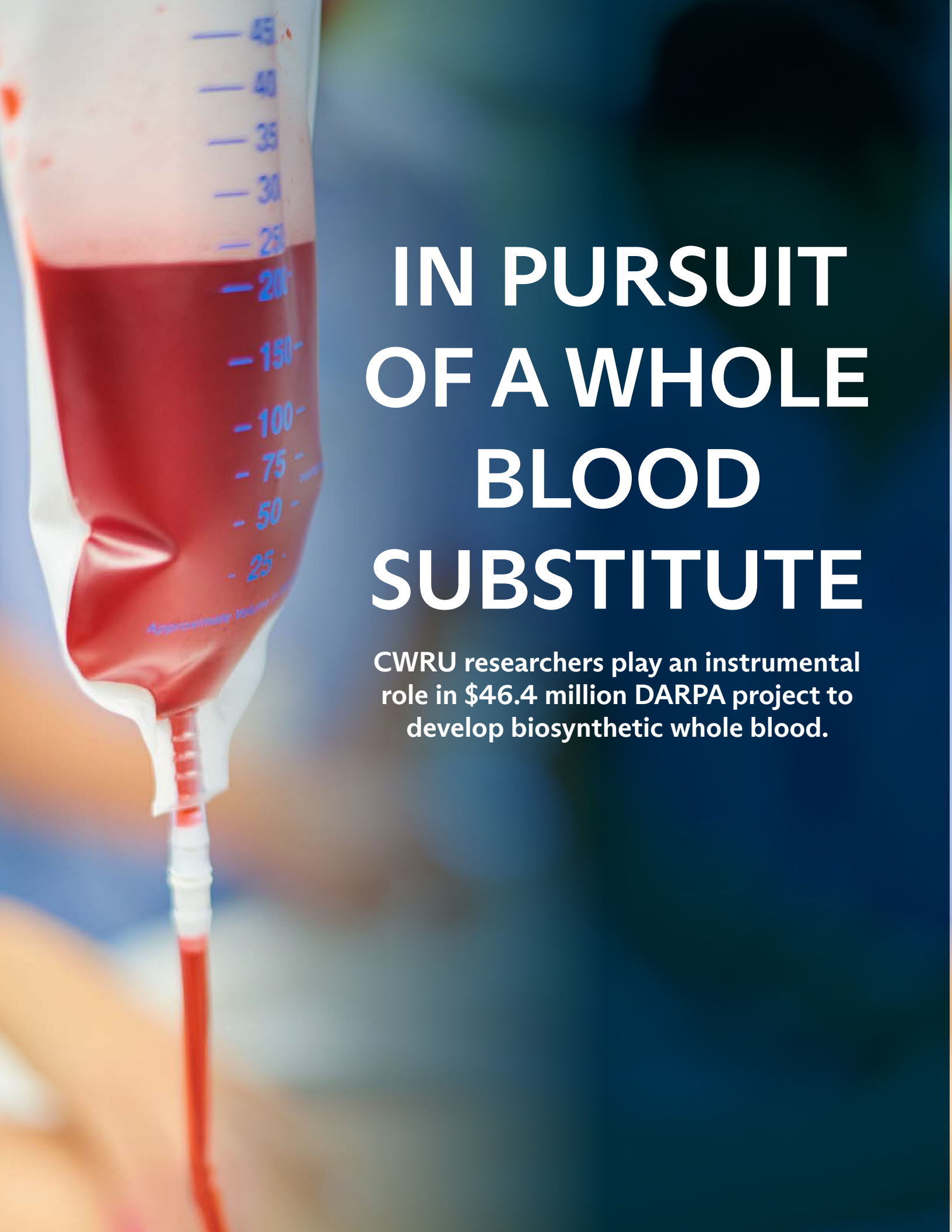
A Focus on Osteoarthritis

The Arthritis Foundation named Cleveland Clinic as the future home for its Osteoarthritis Imaging Center (OIC), which aims to become the country's largest repository for imaging data from post-traumatic osteoarthritis clinical trials and therapies. The OIC will play a critical role in improving care for patients with osteoarthritis, which is the most common form of arthritis, affecting more than 32.5 million people in the United States, according to the Centers for Disease Control and Prevention.

The OIC will coordinate imaging for all future multicenter osteoarthritis clinical trials in the U.S. that are run through the foundation's Osteoarthritis Clinical Trial Network. Images from multiple modalities, including MRI, computed tomography and radiography, will be sent to the OIC for interpretation and analysis. Researchers and physicians can reference them in a central location for future studies and patient care.

"By establishing a large, central hub, we can provide the support needed to collect the 'big data' in a standardized manner that researchers need to solve problems and develop new treatments," says Xiaojuan Li, staff in the Lerner Research Institute Department of Biomedical Engineering and director of the Program of Advanced Musculoskeletal Imaging at Cleveland Clinic. "The OIC is designed to provide core services for institutions conducting clinical trials that otherwise might need to be subcontracted out at a higher expense."

During phase 1 of the $2.5 million grant from the Arthritis Foundation, researchers at Cleveland Clinic will build the infrastructure for gathering and archiving images from sites around the country.



IN PURSUIT OF A WHOLE BLOOD SUBSTITUTE

CWRU researchers play an instrumental role in $46.4 million DARPA project to develop biosynthetic whole blood.

Every two seconds someone in the U.S. needs a blood transfusion, according to the American Red Cross.

"Blood transfusion is a highly critical, life-saving clinical procedure for a variety of patients, including people bleeding out from severe injury or undergoing surgery, as well as those whose native blood doesn't function adequately due to disease or medication effects," says Anirban Sen Gupta, the Wallace R. Persons Endowed Professor of Engineering in Case Western Reserve University's Department of Biomedical Engineering. "The transfusion logistics become highly problematic when you realize that blood availability is completely donor driven and there is often a paucity of donors, especially in scenarios such as the recent COVID pandemic."

Anirban Sen Gupta

Case Western Reserve University is one of several universities and industry partners working on a solution as part of a four-year, $46.4 million project funded by the Defense Advanced Research Projects Agency (DARPA). The project aims to develop a bioartificial whole blood surrogate.

The blood surrogate will combine, evaluate and optimize three biosynthetic components that mimic the function of platelets, red blood cells and plasma respectively. An additional focus of the project is to establish that the optimized artificial blood can be freeze-dried and stored as a powder under various environmental conditions so that it can then be reconstituted on demand using saline.

"There's been a lot of research on artificial blood for decades, ramping up during the AIDS pandemic in the 1980s. But most of the work in the past focused on a single component – red blood cells," says Sen Gupta. "This is indeed the world's first attempt to try to make artificial whole blood that includes mimicking other critical components, such as platelets and plasma."

Tackling Challenges in Blood Donation and Transfusion

The researchers hope that creating a viable blood surrogate will overcome several challenges associated with donor-derived blood usage. First is availability: Blood product need and utilization often outpace blood donations. Logistics and portability present another hurdle.

"Even if you get ample donations, you have to type match blood, bank it and get it where it needs to be," says Sen Gupta. While most transfusions occur within hospitals, in some scenarios – such as traumatic bleeding due to injury – the earlier you can transfuse the blood, the better the survival outcomes.

"Whether it's a civilian car accident or a military battlefield, access to blood needs to be rapid. Ideally, the blood should be taken to the patient rather than waiting for the patient to come to the hospital," says Sen Gupta.

Finally, blood has a fixed shelf life. Whole blood can be stored between 1 and 6 degrees Celsius for approximately a month. Frozen plasma is viable for several months, while cooled platelets have a shelf life of approximately two to three weeks.

"If you take into account the shortage in donation and limited shelf life, the challenges are amplified," says Sen Gupta. "We just don't have enough blood, and even if we do, we can't stockpile it."

The DARPA project strives to address all of these issues and develop a synthetic system that functions like biologic blood, can be manufactured at large scale, doesn't require type matching and can be freeze-dried, stored and transported anywhere in the world.

"All of these are hard problems, and we are trying to solve them in parallel," says Sen Gupta.

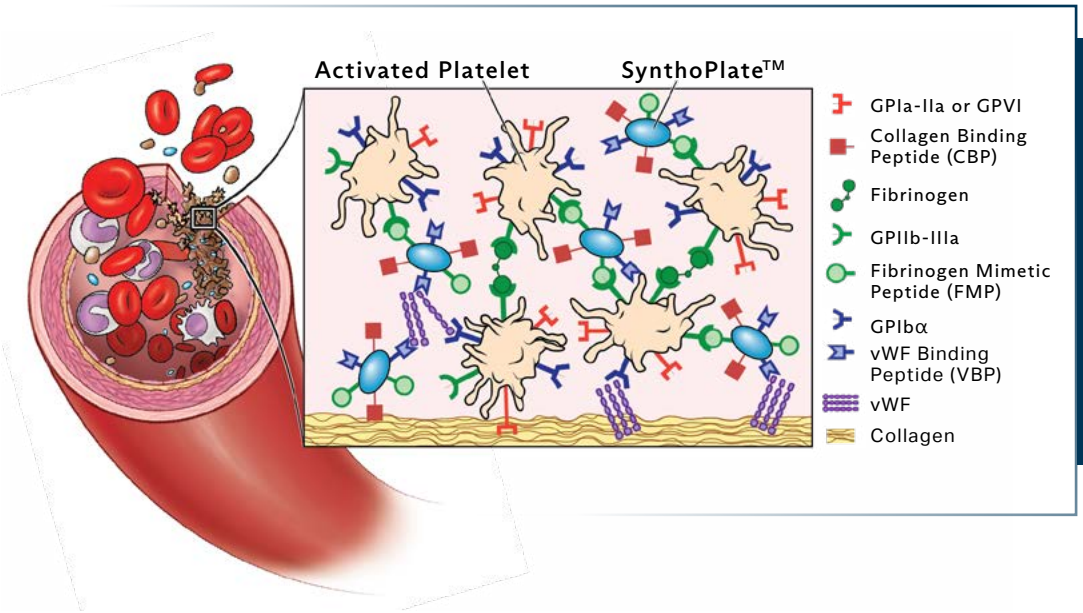
Partner Roles

The components being combined and tested in the whole blood surrogate include:

- SynthoPlate™, a synthetic hemostatic agent developed by Sen Gupta and licensed to Haima Therapeutics
- ErythroMer, a dried red blood cell substitute made by KaloCyte
- Freeze-dried plasma from Teleflex

While the individual components are important, it's imperative that they work together to mimic the critical functions of real blood.

"In a reductionist view, we can boil down the function of blood to three main roles – oxygenation, hemostasis and hemodynamics," says Sen Gupta. "Our role at



Schematic depiction of the mechanism of action of SynthoPlate to mimic and cooperate with the adhesive and aggregatory functions of natural platelets to form a hemostatic clot.

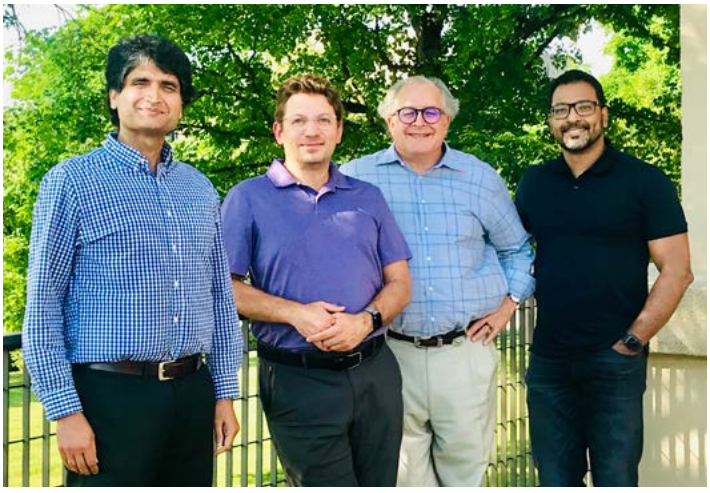
CWRU is to integrate all of the artificial components and use a multitude of in vitro techniques and methods to evaluate and optimize hemostasis, which is our natural ability to form a clot to stop bleeding."

Researchers at the University of Maryland are studying oxygenation, and a team at the University of California San Diego is examining hemodynamics. After the universities have agreed on an optimal formulation, it will be studied in vivo at the University of Pittsburgh, which is also responsible for blood banking and comparing the artificial whole blood to stored real blood.

The four-year DARPA project has set ambitious non-inferiority criteria: Each of the three domains – oxygenation, hemostasis and hemodynamics – must be 90% as effective as donor-derived stored blood used in transfusions. There are intermediate goals of 60% functionality at the end of year one, 70% at the end of year two and 80% at the end of year three. Case Western Reserve University has met the 60% non-inferiority margin for hemostasis within the first year, which ended in January 2024.

Analyzing Clot Formation

Now in the second year of the project, Sen Gupta's laboratory continues to conduct performance analyses of the blood surrogate. Meanwhile, safety parameters are being studied in the laboratories of three co-investigators: Harihara Baskaran, chair of the Department of Chemical Engineering; Umut Gurkan, William J. Austin Professor of Engineering in the Department of Mechanical and Aerospace



From left: Harihara Baskaran, Umut Gurkan, Allan Doctor (lead principal investigator on the DARPA project from University of Maryland) and Anirban Sen Gupta.

Engineering; and Pedram Mohseni, Goodrich Professor of Engineering Innovation and chair of the Department of Electrical, Computer and Systems Engineering.

The performance analyses examine various aspects of clot formation, including how soon the clotting begins, how fast the clot grows and whether the clot remains stable or breaks off.

"Ultimately, the artificial blood system is going to be in circulation in a human body, so it is important that it doesn't cause any kind of harm – a negative immune response, unnecessary clotting or altering viscosity and flow velocity through the blood vessel," says Sen Gupta. "All of these are safety parameter analyses that we are studying in parallel."

Each week, the researchers perform multiple experiments to compare human donor-derived blood to engineered artificial blood. The experiments:

- Measure the kinetics, robustness and stability of clotting
- Image the cellular and molecular mechanisms of blood clotting in real time
- Assess the rheology of flowing blood in physiology, simulating microfluidic systems
- Investigate any possible harmful effects of the blood on endothelial cells and immune cells

Scaling Up and Deploying the Product

While universities are analyzing oxygenation, hemostasis and hemodynamics, industry partners are working on the logistics of producing synthetic whole blood at scale.

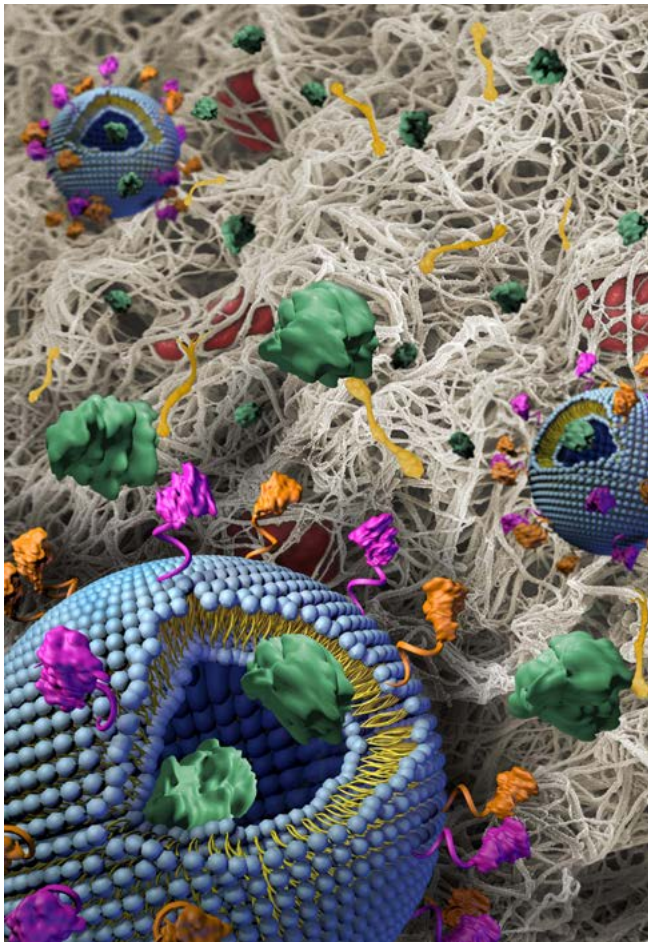
"We have to confirm that scale up doesn't affect the function. It might work in one milligram, but what if it fails in one gram scale?" says Sen Gupta. "Also, what if a freshly made system works great, but when you freeze dry it and then reconstitute in saline it doesn't work that well anymore?"

Sen Gupta and the other researchers communicate regularly with teams from Haima Therapeutics, KaloCyte and Teleflex and refine the blood surrogate formulations as they strive to create a functioning whole blood substitute. In addition, the Southwest Research Institute is spearheading efforts to scale up production and create sterilized packaging for rapid deployment.

The lifesaving potential of synthetic blood is vast. Soldiers could carry freeze-dried blood in their modular lightweight load carrying equipment (MOLLE) to treat injury on the battlefield. Ambulances could stock it for emergency medical personnel to give blood transfusions to people following car accidents, mass casualty events or other emergencies. Hospitals could stock artificial blood for on-demand use in surgeries, injuries, disease and bleeding disorders.

"All of the partners in the consortium are excited to be part of this historic effort," says Sen Gupta. "This endeavor is the first to invest in integrating the oxygen-carrying function with clot formation and hemodynamics to create a product that is functionally close to whole blood."

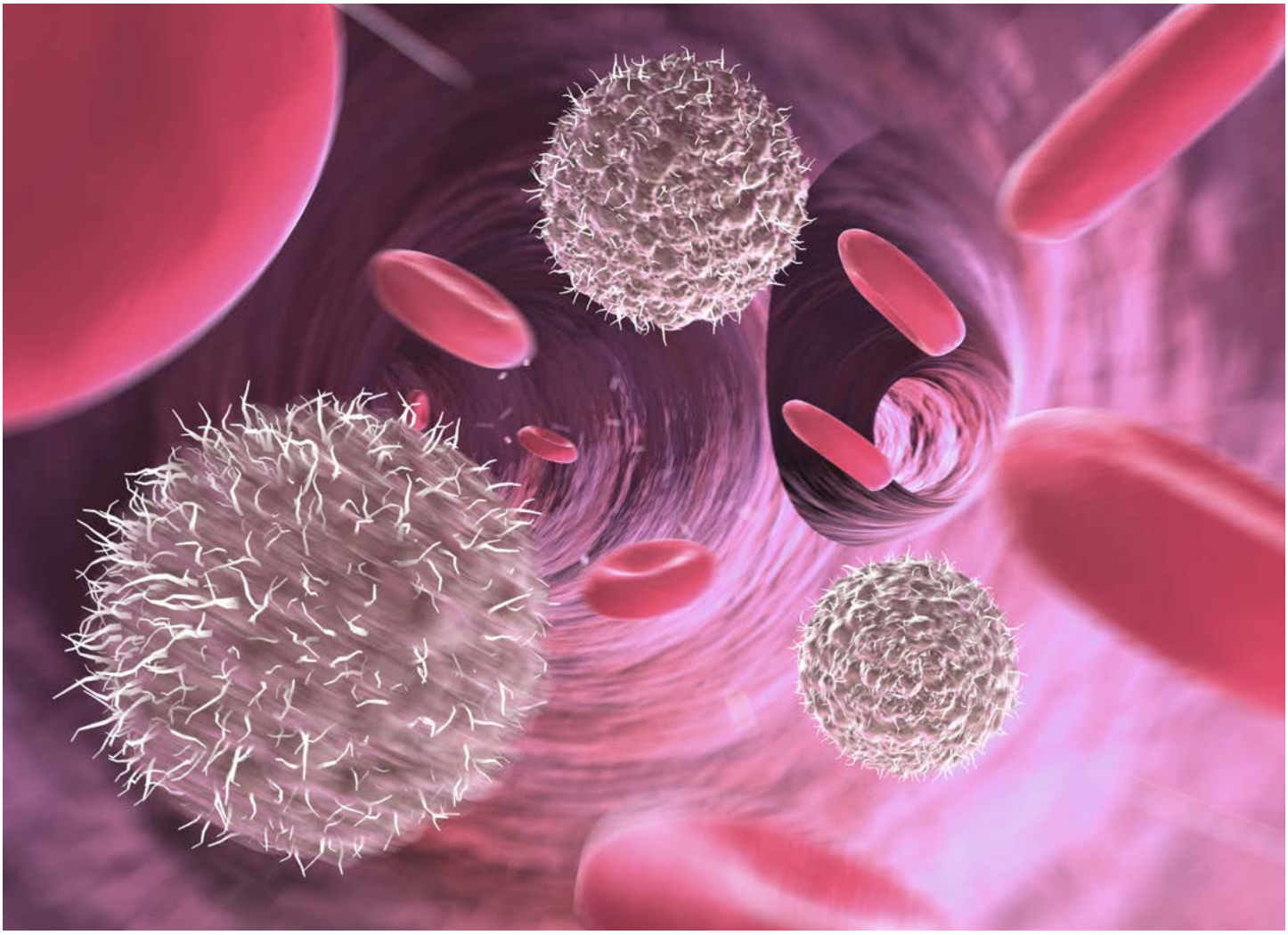
Sen Gupta and researchers in his laboratory discuss viscoelastometry analysis results for the whole blood analog.



An artist's rendering of platelet-mimicking liposomal nanoparticles embedded in a scanning electron microscopy image of a fibrin-rich blood clot.

HARNESSING THE POWER OF THE IMMUNE SYSTEM

Newly appointed professor leads a team developing biomaterials to govern immune cell responses and affect disease outcomes.



"When you learn, teach. When you get, give."
- Maya Angelou

Abhinav Acharya, Assistant Professor of Biomedical Engineering at Case Western Reserve University

Every Monday morning, Abhinav Acharya emails a motivational quote to team members in his lab and other colleagues.

"I eagerly anticipate this dose of wise and meaningful advice, which sets a positive tone for the start of each week," says Joslyn Mangal, who earned her doctorate from Arizona State University in 2022 under the mentorship of Acharya and now works as a principal investigator at ImmunoMetabolix, one of his start-up companies.

Acharya's positivity, along with his passion for science and commitment to collaboration, have contributed to his rise in the burgeoning field of immunoengineering. Existing at the intersection of immunology and engineering, the discipline strives to create new technologies to better understand and modulate the immune system.

Last fall, Acharya joined Case Western Reserve University as assistant professor in biomedical engineering and a member of the Case Imaging Program in the Case Comprehensive Cancer Center.

"I want to grow the immunoengineering area, and there's no better place than Case to do it," says Acharya. "The university offers unique access to world-class engineers, experts in the School of Medicine and clinical collaborators in leading healthcare systems, such as Cleveland Clinic and University Hospitals."

Interest in Immunometabolism

As an undergraduate student in metallurgical engineering at the National Institute of Technology in India, Acharya became intrigued by how materials implanted in the body – hip and knee replacements, dental implants and so on – interacted with different biological systems.

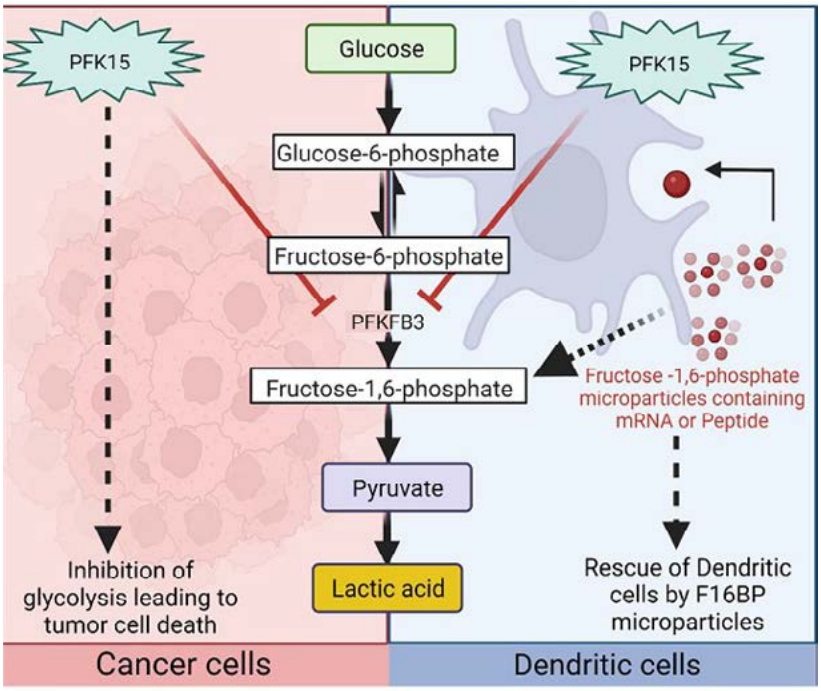
"One of the first things that biomaterials see is the immune system, which touches every other system in the human body. That really attracted me to the field of immunoengineering," says Acharya. "I can collaborate with folks who work not just in immunology, but in other systems like the endocrine and renal system that interact with the immune system. We work together to ask and answer really difficult questions."

Acharya earned a master's degree and PhD in materials science and engineering from the University of Florida, then completed postdoctoral fellowships at the Georgia Institute of Technology and the University of California, Berkeley. After serving as a postdoctoral researcher at the University of Pittsburgh, he was an assistant professor in chemical engineering at Arizona State University before joining Case Western Reserve University. In each of these stops, Acharya expanded his network of collaborators and the scope of his research.

"Abhi's lab comes up with out-of-the-box ideas that are practical and have great translational value," says Sahil Inamdar, who was the first PhD student to graduate from Abhi's lab. "In the last five years, he has created a niche in immunoengineering at the cross section of biomaterials, metabolism, immune modulation and vaccine development for various diseases."

Cancer Immunotherapy Meets ImmunoMetabolism

The drug PFK15 reduces glucose uptake in cells, including cancer cells (shown left). However, dendritic cells — the body's decision-making immune cells — are fed with F16BP microparticles and have active glycolysis, even in the presence of PFK15 (shown right). These microparticles allow immune cells to generate energy and function, leading to robust cancer immunotherapy.



A Three-Pronged Approach

Researchers in Acharya's lab at Case Western Reserve University are focused on three main areas – designing biomaterials, engineering the immune system's metabolism and developing clinical applications.

"We utilize biomaterials to modify the metabolism of immune cells and see if it affects the disease outcome with the ultimate goal of generating translatable products to treat chronic inflammatory conditions, autoimmune diseases, cancer and other conditions," says Acharya.

The team has designed several polymers as vaccine components that can modify metabolism. These include a vaccine for rheumatoid arthritis, which has been patented and licensed.

"We are also developing vaccines for traumatic brain injury (TBI) that soldiers, football players and other at-risk people can get before they have trauma and reduce chronic inflammation-associated symptoms after TBI," says Acharya.

After arriving at Case, Acharya initiated a microelectrode implant project with Jeff Capadona, professor in the Department of Biomedical Engineering and the School of Medicine. Capadona's lab develops advanced, bio-inspired materials for brain interfaces to facilitate neural recordings. One of the impediments to widespread adoption of neuroprosthetic devices is the unreliability of chronic neural recordings.

"The immune system is constantly infiltrating the microelectrode implant site and affecting recordings," says Acharya. "We are trying to educate the immune system to develop receptors that recognize the microelectrode – a completely foreign material – as part of your own body so you don't start attacking it." That would extend the life of the implanted microelectrodes.

Clinical and Educational Impact

The lab's projects blanket a vast swath of conditions, including traumatic brain injury, multiple sclerosis, rheumatoid arthritis, lymphoma and melanoma, with the ultimate goal of helping people.

"From the start I have made it a priority for my lab that when we address a problem and develop a formulation, we always keep in mind the final clinical impact," says Acharya. That focus on translational science has contributed to the spinoff of technologies and launch of two startup companies.

ImmunoMetabolix is dedicated to upscaling and commercializing metabolite-polymer technologies for treating immune-mediated diseases that could stand alone or work in tandem with existing immunotherapies, such as checkpoint inhibitors, vaccines and chimeric antigen receptor (CAR) therapy. VaderBio is focused on developing interleukin-based therapies for treatment of autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis.

As the Acharya lab develops more technologies – and graduates more students – its influence on the immunoengineering field will continue to grow. After earning his PhD in 2022, Inamdar joined Khloris Biosciences as a pre-clinical vaccine development specialist helping the company advance the use of induced pluripotent stem cells (iPSCs) as potential vaccines for cancer treatment.

"I am in industry today because of Abhi's mentorship and guidance," says Inamdar. "He has a great entrepreneurial acumen, which has trickled down to all his students." That includes Mangal, whose responsibilities at ImmunoMetabolix include writing and editing grants and collaborating with researchers to publish manuscripts.

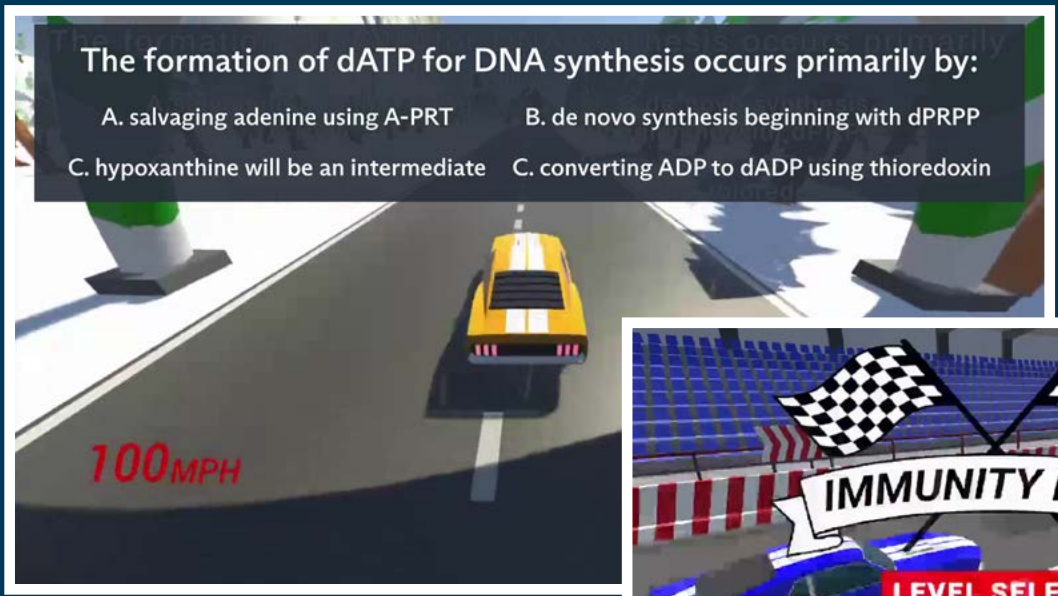
"Abhi fosters a passion for research by empowering students to formulate their own ideas," she says. "This approach ensures that students are not only passionate and invested in their work, but also develop skills that extend beyond their graduate careers."

To reach even more students, Acharya created an undergraduate course on immunoengineering at Arizona State University. Launched during the COVID-19 pandemic, it garnered a lot of interest. He hopes to introduce the course at Case Western Reserve University when he begins teaching in the fall.

Focus on Growing the Field

Acharya can boast many individual accomplishments, including 17 patents and more than 55 journal publications. However, for him the goal is to grow the field and expand the horizon of immunoengineering.

"There are people working in neurology, immunology and biomaterials – all on the fringes of immunoengineering," he says. "If we propagate the field, we can bring all those people into the fold and grow it exponentially."



Abhinav Acharya uses a video game to teach undergraduate students about different metabolic pathways, including Krebs cycle, glycolysis, amino acids and lipid oxidation pathways.

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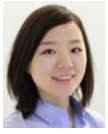

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