



RESEARCH: IMPACTING AND EXPANDING KNOWLEDGE



MIDWESTERN UNIVERSITY

Tomorrow's Healthcare Team

WWW.MIDWESTERN.EDU

555 31st Street | Downers Grove, Illinois 60515

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2020 – 2021

Message from the President



Scientific exploration has always been a critical focus at Northwestern University. Research efforts like the ones you will read about in these pages are pushing back the limits of scientific knowledge. From exploring new medications and therapies, to creating models of population movements and environmental factors to understand disease vectors, to delving into the fossil record to understand how human and animal life develops in and adapts to various environments over time, our faculty, staff, and students are enthusiastically setting themselves on the path to discovery.

We believe as a University that this search for knowledge is worthy, professionally and educationally, to the extent that we have invested millions of dollars in facilities, internal grants, staff support, and other resources. Together with entities such as the National Institute of Health (NIH), the Departments of Health Services in Illinois and Arizona, the National Science Foundation, and many others who have funded our researchers, we are committed to providing an environment that emboldens our faculty and students to strive for the knowledge and insight that will make them better healthcare

professionals. That commitment has been noticed by our peers in the healthcare industry, as we have seen our research funding increasing every year.

I urge you to read this Research Annual Report closely. Get to know our wonderful faculty and students involved in research initiatives. Discover some of our groundbreaking facilities and research centers. Share in our pride in the significant place our faculty, staff, and students occupy in the ongoing challenge of expanding our understanding of global health. You will find that tomorrow will be in good hands, thanks to what we are working toward today.

Sincerely,

A handwritten signature in black ink that reads "Kathleen H. Goepfinger, Ph.D." The signature is fluid and cursive.

Kathleen H. Goepfinger, Ph.D.
President and Chief Executive Officer, Northwestern University

EXPANDING RESEARCH AND IMPACTING KNOWLEDGE



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GRANTS: \$3,667,628 in National Institute of Health Awards (NIH)

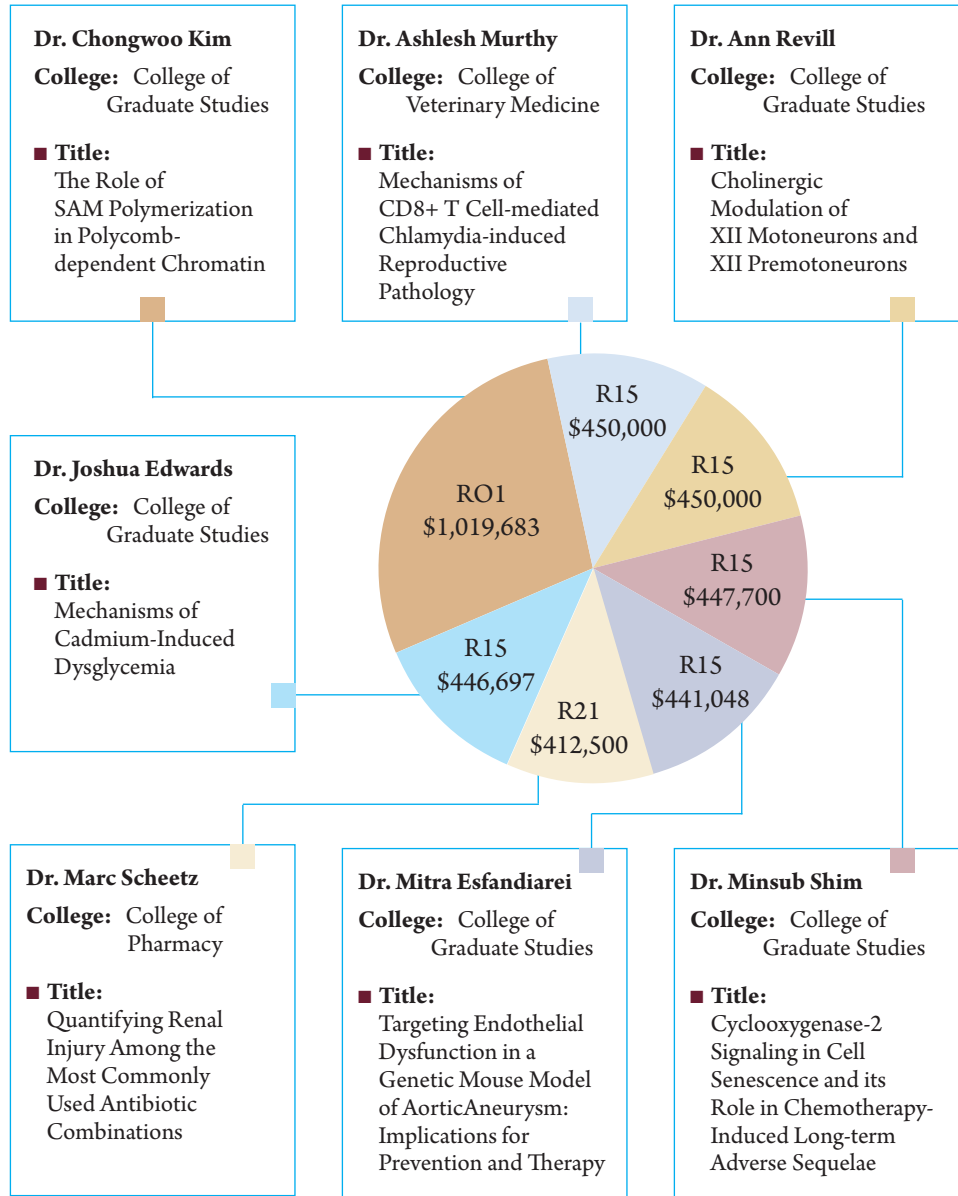
Principle Investigators and Projects Awarded Grants Exceeding \$400,000:

\$31.9 MILLION
Commitment to Research Activities*
 in Fiscal Year 2020

\$3.21 MILLION
for Extramural Active Grant Funding
 in Fiscal Year 2020

\$1.34 MILLION
in Extramural Funding Expenditures
 in Fiscal Year 2020

103 STUDENT RESEARCH FELLOWSHIPS
budgeted at >\$499,000
 in Fiscal Year 2020



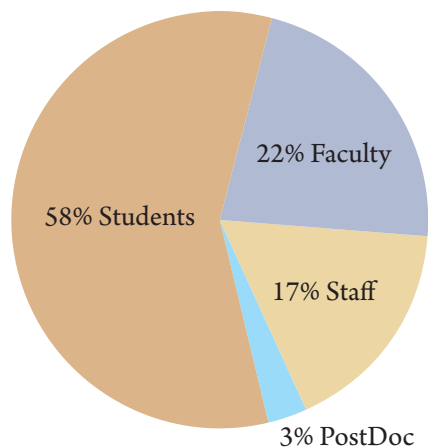
* Includes direct and indirect costs associated with hard money technicians, research departments (e.g. ORSP, IHI, Animal Resources, etc.), percentage of time commitment of faculty, their lab space and direct supply and capital needs to perform research. For FY20, this equates to 7.5% of the university budget.

■ Research Facilities Spotlight – Downers Grove Campus



Core Facility Provides Research Hub for Students, Faculty

IL-CORE Facility Users



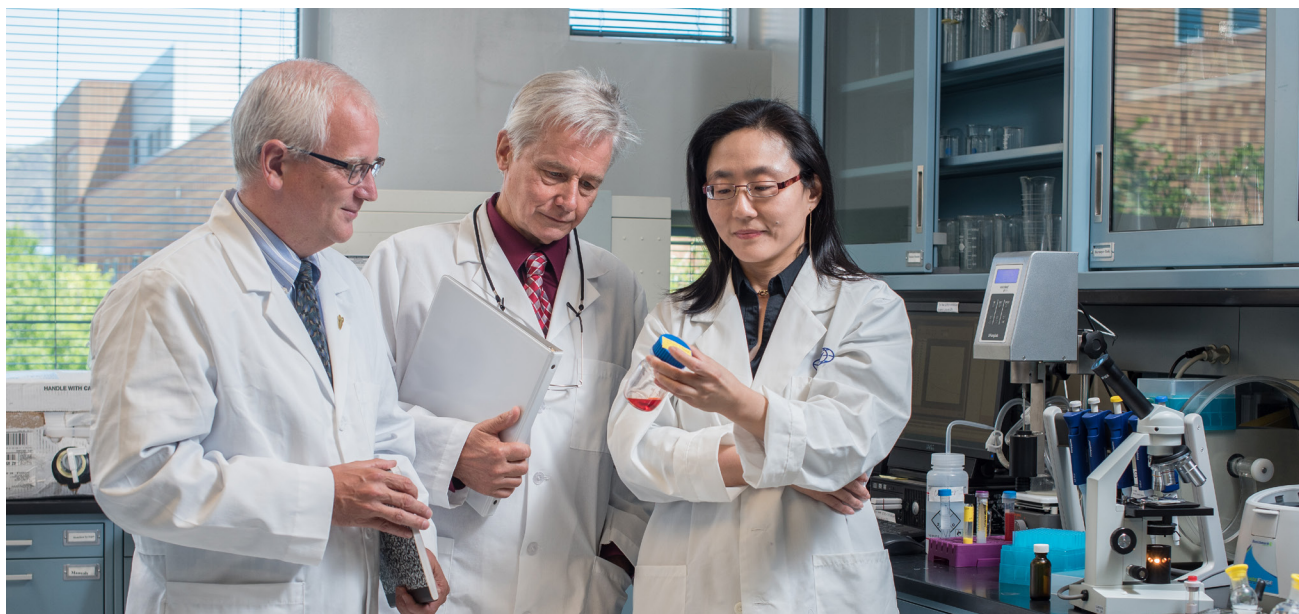
The Midwestern University IL-Core Facility houses state-of-the-art instrumentation that is available to any Midwestern University faculty, staff, or student researcher. This shared equipment laboratory space is located in Science Hall on the Downers Grove Campus. It is actively funded by Midwestern University to support research, foster collaborative projects, drive scientific innovation, and engage our community by hosting STEM education programs.

The IL-Core Facility opened in January 2018 and has been adding new instruments every year. It currently has more 20 pieces of equipment that allow researchers to conduct a wide range of scientific experiments. Since its inception, the IL-Core Facility has seen over 145 users and the majority of those users have been students.

For more information about these and other research projects, visit the Research section on the Midwestern University website at: <https://www.midwestern.edu/research.xml>.

MWU Grants Funded from \$100,000 - \$400,000

Investigator/s	College(s)	Title	Total	Agency
Eckman, D., Jones, C., Jones, T.B., Vallejo-Elias, J. Virden, T. & Powell, J.	CGS & CHS-GD	Cerebrovascular Dysfunction and Cognitive Decline in Aging APOE2, APOE3 and APOE4 Targeted-Replacement Mice	\$225,000	AZ Dept. of Health Services through the AZ Biomedical Research Commission
Ellermeier, J.	CGS	Genetic Regulation of the Twin Arginine Translocation System in Salmonella enterica serovar Typhimurium	\$150,000	NIH-R03
Jadavji, N.	CGS	Identification of Developmental Factors Involved in Ischemic Stroke Outcomes in Adulthood and Old Age	\$152,735	American Heart Association
Riede, T.	CGS	Collaborative Research: Evolution of Long-distance Communication in Vocal Rodents	\$193,774	National Science Foundation
Riede, T.	CGS	The Role of Vocal Ligament in Fundamental Frequency and Adduction Control	\$201,055	NIH-R01 Subcontract from the University of Utah
Townsend, K.E.B.	CGS	Collaborative Research: After the Bridgerian Crash - An Integrated Analysis of Mammalian Paleocommunities and Paleocologies During the Middle Eocene	\$239,596	National Science Foundation
Elbayoumi, T. and Yao, M.	CPG	Atrial Fibrillation Strategically Focused Research Network: Atrial Substrate in Atrial Fibrillation and AF-associated Brain Disease	\$126,979	American Heart Association Subcontract from Northwestern University
Scheetz, M.	CCP	A Retrospective Study to Understand the Risk Factors/Drivers of "Inappropriate" Antimicrobial Use and the Performance Evaluation of a Clinical Decision Support Tool that Facilitates Prediction of Outbreaks of Inappropriate Antibiotic Use	\$159,835	Merck Sharp & Dohme Corp. with a Subcontract to the University of Michigan and Wayne State University
Scheetz, M.	CCP	AKI001 Vancomycin (MEEK) and AKI002 Liposomal Vancomycin	\$124,718	Nevakar, Inc.
Vasudevan, B.	AZCOPT	A Multi-center, Double-masked, Randomized, Placebo-controlled, Phase 3 Study of the Safety and Efficacy of Atropine 0.1% and 0.01% Ophthalmic Solutions Administered with a Microdose Dispenser for the Reduction of Pediatric Myopia Progression (The CHAPERONE Study)	\$313,000	Eyenovia
Vasudevan, B.	AZCOPT	Effect of LipiFlow on Ocular Surface Disease Management with Cataract Surgery	\$273,000	Johnson & Johnson Surgical Services
Rice, S.	CCO	A Multi-center, Double-masked, Randomized, Placebo-controlled, Phase 3 Study of the Safety and Efficacy of Atropine 0.1% and 0.01% Ophthalmic Solutions Administered with a Microdose Dispenser for the Reduction of Pediatric Myopia Progression (The CHAPERONE Study)	\$313,000	Eyenovia
Woods, C. & VandenBerg, C.	IHI	Medical Device Study in Patients with Cardiovascular Disease	\$100,000	Medical Device Sponsor (Confidential)



Nanomedicine Center Models Collaboration, Research, and Mentorship

The goals of the Center are to:

- Advance the knowledge and application of the next generation of personalized and targeted medicines;
- Enhance scholarly activity and research to support the education of future healthcare team professionals;
- Solidify collaboration of interdisciplinary faculty teams to actively compete for and attract extramural grant funding;
- Coordinate MWU preclinical research training programs; and
- Establish collaborative partnerships with regional pharmaceutical industry players and leading clinical practices.

The Midwestern University Nanomedicine Center of Excellence in Translational Cancer Research (Nanomedicine COE-TCR) was established by the University's College of Pharmacy, Glendale in 2016, and expanded in 2017 as a multidisciplinary collaborative research center across the University's two campuses in Glendale, AZ and Downers Grove, IL

As a component of the University's One Health Initiative, the Nanomedicine COE-TCR integrates nanotechnology design, application, and biomedical research to serve Midwestern University as a consortium for collaborative faculty research efforts, support the education of its students, and impact human and animal patients.

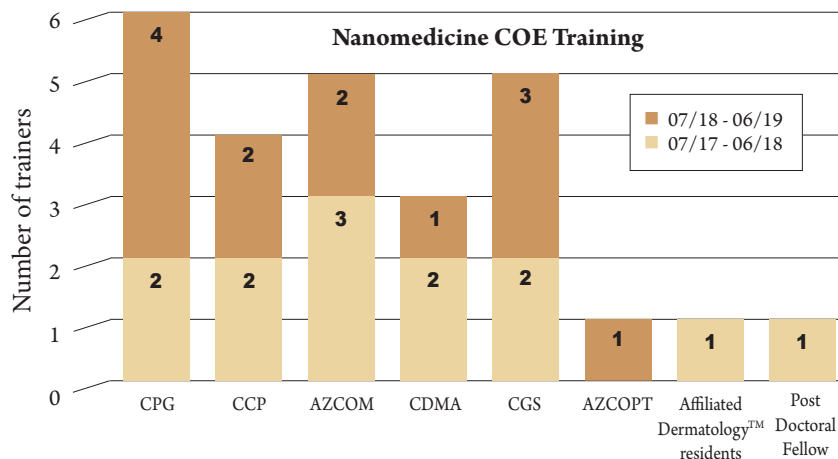
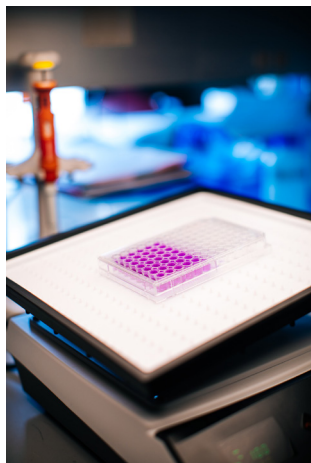
Building upon the expertise and international reputation of its pharmacy faculty in nanomedicine and drug targeting, the Center is co-directed by College of Pharmacy-Glendale faculty members Tamer Elbayoumi, Ph.D., M.Sc., Professor of Pharmaceutical Sciences, and Volkmar Weissig, Ph.D., Chair of Pharmaceutical Sciences. There are eight active principal investigators from four different colleges, including the College of Pharmacy (both campuses), the College of Graduate Studies (both campuses), the Arizona College of Osteopathic Medicine, and the College of Dental Medicine-Arizona.

The Center also provides mentorship, and has trained over 40 students, residents, and faculty since 2017. Collectively, between July 2017 and December 2019, its faculty have published 15 peer-reviewed manuscripts, one patent, and one edited book, with an additional five publications anticipated soon.

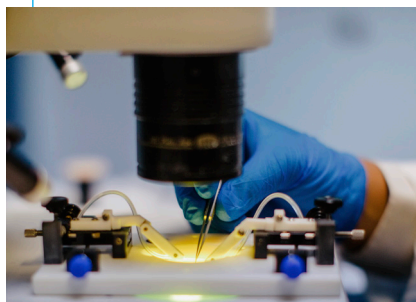
The Nanomedicine COE-TCR has received more than \$300,000 in extramural funds and submitted over \$4 million in extramural grants. Multiple joint Nanomedicine- COE projects have received the Annual Multidisciplinary Research Stimulus Award five times since 2015, for both the AZ and IL campuses.

Primary multidisciplinary research areas currently include:

- Targeted nanoscale therapeutics for solid, cutaneous and hematologic tumors;
- Cancer and cardiovascular diseases;
- Nanobiomaterials for chemotherapy of periodontal and oro-pharyngeal lesions; and
- Hybrid nanocoated 3D-printing technologies for tissue bioengineering and biocompatible prosthetic devices for ocular and upper limb differences.



■ The Potential Role of Environmental Toxin's in Diabetes



“In a study of the U.S. population, 25% of individuals who were diabetic or prediabetic had elevated urinary cadmium levels.”



Project: Mechanisms of Cadmium-Induced Dysglycemia

Principle Investigator: Joshua R. Edwards, Ph.D., College of Graduate Studies, Professor, Pharmacology

Co-investigators: Michael Fay, Ph.D., Associate Dean, College of Graduate Studies - Downers Grove; Walter Prozialeck, Ph.D., Professor, Pharmacology; Latha Malaiyandi, Ph.D., Associate Professor, Anatomy; Kirk Dineley, Ph.D., Professor, Pharmacology; and Malek El Muayed, M.D., Assistant Professor of Medicine, Northwestern University.

Grant: \$446,697 NIH-R15 (AREA)

Dates: 8/15/2017 to 7/31/2020

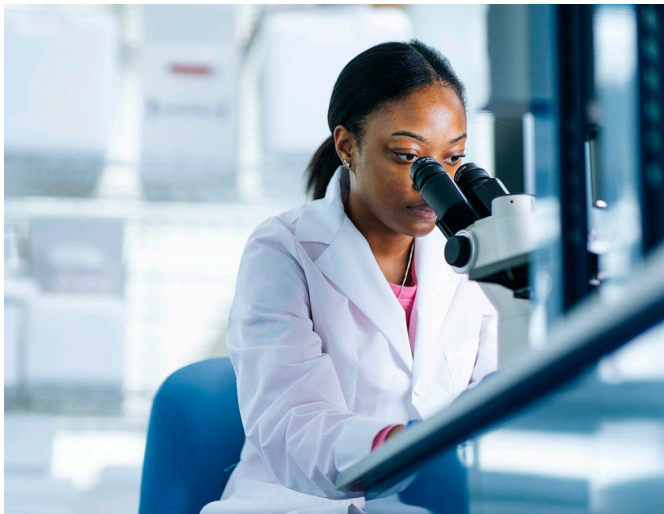
Project Summary:

Exposure to the widespread environmental contaminant, cadmium, is associated with diabetes and prediabetes. The studies will investigate the cellular mechanisms by which cadmium contributes to the onset of diabetes, an urgent and growing public health concern.

Cadmium is a ubiquitous environmental and industrial pollutant that currently ranks seventh on the US EPA/ATSDR Priority List of Hazardous Substances and is a known human carcinogen that causes kidney, liver, and bone damage. Cadmium also disrupts blood glucose levels. In a study of the U.S. population, 25% of individuals who were diabetic or prediabetic had elevated urinary cadmium levels. It is unknown how cadmium disrupts blood glucose levels; however, cadmium exposure is associated with altered insulin levels in individuals with

occupational exposure to the toxin. Results from these studies will determine the cellular pathways by which cadmium causes impaired insulin secretion in pancreatic islets, a cluster of cells in the pancreas that produce hormones such as insulin that determine blood glucose levels. The investigators will also gain knowledge in how pancreatic islets function normally in the absence of toxins like cadmium.

“Since being funded by NIH in 2017, well over a dozen Midwestern University students from our osteopathic medicine, dental medicine, pharmacy, and biomedical science programs have directly contributed to these studies or utilized tissues generated from these experiments. Hopefully, this will have a lasting impact on our students by encouraging life-long learning and be the impetus that spawns their own future research program in their chosen profession,” Dr. Edwards said.

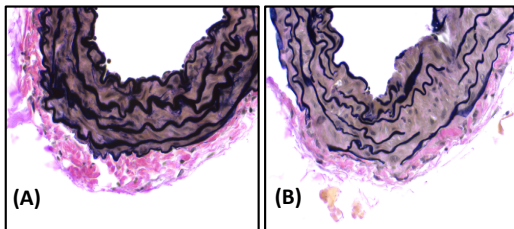




Finding New Directions for Aneurysm Treatments

“Every year, many people die from aortic aneurysm, and over the last decade, the average age for aneurysm has decreased significantly.”

Staining Morphology of elastin fibers in the cross section of aortic wall



Representative images of cross-sections of ascending aorta from (A) control mouse and (B) mouse with aortic aneurysm. Disorganization and fragmentation of elastin fibers within the aortic wall are evident.

Project: Targeting Endothelial Dysfunction in a Genetic Mouse Model of Aortic Aneurysm: Implications for Prevention and Therapy

Principal Investigator: Mitra Esfandiarei, Ph.D., College of Graduate Studies, Associate Professor, Biomedical Sciences

Co-investigators: Pascal Bernatchez, Ph.D., Associate Professor, Department of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia (Vancouver, BC)

Grant: \$441,048 NIH-R15 (AREA)

Dates: 1/15/2019 to 12/31/2021

Project Summary:

An aortic aneurysm is an abnormal bulge that occurs in the wall of the major blood vessel (aorta) that carries blood from the heart to the body. Having an aortic aneurysm increases the risk of developing an aortic dissection, which occurs when a tear develops in the inner layer of the wall of the aorta. This causes one or more of the layers of the wall of the aorta to separate, which weakens the wall of the aorta. Every year, many people die from aortic aneurysm, and over the last decade, the average age for aneurysm has decreased significantly.

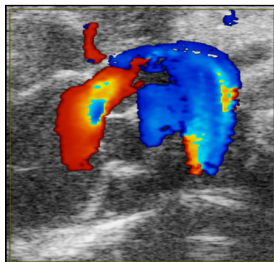
Midwestern University researchers led by Dr. Mitra Esfandiarei are working in collaboration with the Stanford University Connective Disorders Clinic on a parallel study of aortic aneurysm in mice and human patients. “My team utilizes a well-defined genetic mouse model of aortic aneurysm to gain a better understanding of cellular and molecular factors contributing to the development of aneurysm,” says Dr. Esfandiarei. “We are also interested in understanding how different interventions such as diet, physical activity, and known blood pressure lowering drugs such as beta blockers (Atenolol) or angiotensin-II type I receptor blockers (Losartan) may have protective effects by delaying or completely blocking the abnormal changes that occur during aneurysm development.”

The team’s particular focus is on Marfan syndrome (MFS), an inherited disorder that affects connective tissue — the fibers that support and anchor organs and other bodily structures. Marfan syndrome commonly affects cardiac structures including heart valves and blood vessels. The aortic damage caused by Marfan syndrome is called aortic root enlargement, which is a dilation of the area in the heart where the aorta meets the aortic valve that can cause the aortic valve to stretch and leak.

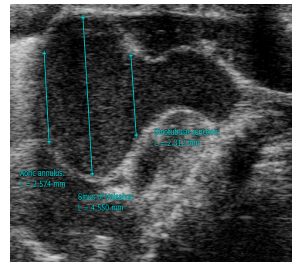
By studying the effects of various treatment vectors on MFS mice – including mild aerobic exercise, existing treatments like Losartan, and other pharmacological and genetic approaches to increase endothelial function, the team hopes to indicate promising new therapeutic directions for treating aneurysm.

“By having unlimited and cost-free access to the state-of-the-art high resolution ultrasound imaging system purchased by Midwestern University, my research team has been able to collect valuable data from the live animal that is comparable to measurements in patients with aneurysm,” Dr. Esfandiarei says. “This will allow for better understanding of the longitudinal changes in blood vessel function and structure as the aneurysm forms and progresses, and facilitates the transfer of our novel findings from the bench to the bedside.”

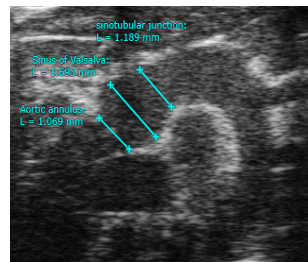
Ultrasound Imaging of the aortic root and arch in a 6-month-old mouse



(A)



(B)



(C)

(A) B-Mode Doppler view of a 3-month-old control mouse aorta, (B) B-Mode view of the aortic root in a 6-month-old control mouse, (C) B-Mode view of the aortic root in a 6-month-old mouse with aortic aneurysm.



■ **Protein Polymers
May Be Key to New
Genetic Therapies**

“A Midwestern University research team is exploring the structural arrangement of SAM polymers to determine whether its polymerization can be controlled, thereby making possible the functional control of SAM polymer-containing proteins themselves.”

Project: The Role of SAM Polymerization in Polycomb-dependent Chromatin Structures

Principal Investigator: Chongwoo Kim, Ph.D., College of Graduate Studies, Associate Professor, Biochemistry and Molecular Genetics

Co-investigator: Nicole J. Francis, Ph.D., Associate Research Professor, Department of Biochemistry, Université de Montréal

Grant: \$1,019,683
NIH-R01, Subcontract to Institut de Recherchers Cliniques de Montréal

Dates: 6/1/2016 to 5/31/2021

Project Summary:

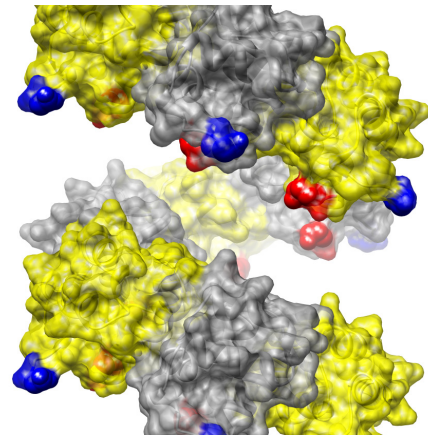
Ongoing research at Midwestern University involving proteins and protein polymers may offer a path toward controlling those proteins, which could result in a new generation of genetic therapies and medications.

Proteins are large biomolecules, or macromolecules, that perform a vast array of functions within organisms, including catalyzing metabolic reactions, DNA replication, responding to stimuli, providing structure to cells and organisms, and transporting molecules from one location to another. Proteins are essential parts of organisms and participate in virtually every process within cells.

Proteins are gene products, created from the “blueprint” of a gene through a process called gene expression. The protein is assembled from information in the gene, and the amount of proteins in a cell is determined from this process. Because proteins act as enzymes, which are needed to catalyze almost all biological reactions, regulation of enzyme activity plays a key role in governing cell behavior.

In living cells, several proteins have the uncommon ability to assemble with multiple copies of itself to form a polymer. One such protein domain, called the Sterile Alpha Motif (SAM) – is found in many proteins, including those involved in gene regulation. A Midwestern University research team is exploring the structural arrangement of SAM polymers to determine whether its polymerization can be controlled, thereby making possible the functional control of SAM polymer-containing proteins themselves.

“There are over 3,000 proteins that contain SAM polymers,” says Dr. Kim. “Despite being in many different proteins with lots of different functions, the SAM polymers share the same architecture, which implies a shared trait. We believe that this shared trait, this helical architecture, may suggest a common way to control or modulate polymerization, which could provide a path toward new genetic therapies and medications that can control gene expression mechanisms across a wide array of cellular functions.”



■ Unlocking the Key to Preventing Drug-Induced Kidney Injury



“This specific research project is relevant to public health because there are few antibiotics available to treat serious infectious diseases and more than 23,000 U.S. patients die annually from antibiotic-resistant infections.”

Project: Quantifying Renal Injury Among the Most Commonly Used Clinical Antibiotic Combinations

Principle Investigator: Marc H. Scheetz, Pharm.D., M.Sc, BCPS, Professor, Pharmacy Practice, College of Pharmacy

Co-investigators: Gwen Pais, Ph.D., Postdoctoral Research Associate, College of Pharmacy; Walter Prozialeck, Ph.D., Professor, Pharmacology; Jack Chang, Pharm.D., Visiting Instructor, Pharmacy Practice; and Peter Lamar, Senior Research Specialist, Pharmacology.

Grant: \$412,500 NIH-R21

Dates: 1/16/2020 to 12/31/2021

Project Summary:

Vancomycin and piperacillin-tazobactam are two of the most common antibiotics given to critically ill adults, and this combination has been clinically reported to significantly worsen acute kidney injury. It is critical to understand if the kidney injury is real or is a false positive due to surrogate limitations of serum creatinine. Dr. Scheetz's lab was the first to identify that clinical studies may have inappropriately over-estimated the increased kidney injury risk when vancomycin and piperacillin-tazobactam are given together. His research seeks to identify the mechanisms of realized toxicity and identify strategies to avoid patient toxicity. Dr. Scheetz employs pre-clinical, clinical, and computer-based modeling approaches to solve these problems.

Ultimately, the researchers believe that strategies and therapies identified in this study will have broad application to prevent drug-induced

kidney injury elsewhere. Drug-induced kidney injury is ultimately preventable or can be greatly minimized. This is important since drug-induced kidney injury shortens patients' lives and compromises their quality of life.

“This specific research project is relevant to public health because there are few antibiotics available to treat serious infectious diseases and more than 23,000 U.S. patients die annually from antibiotic-resistant infections. It is imperative to make our current antibiotics safer and ensure that older antibiotics remain viable because few new antibiotics are being produced,” Dr. Scheetz said. “Vancomycin and piperacillin-tazobactam are two of the most common antibiotics given to critically ill adults, and this combination has been clinically reported to significantly worsen acute kidney injury. We seek to understand if this is true and to develop novel strategies and treatments to make our antibiotics safer for patients,” he added.





MIDWESTERN UNIVERSITY

Tomorrow's Healthcare Team

Downers Grove Colleges

CHICAGO COLLEGE OF
OSTEOPATHIC MEDICINE

COLLEGE OF PHARMACY,
DOWNERS GROVE

COLLEGE OF DENTAL MEDICINE - ILLINOIS

CHICAGO COLLEGE OF OPTOMETRY

COLLEGE OF HEALTH SCIENCES

PHYSICIAN ASSISTANT

PHYSICAL THERAPY

OCCUPATIONAL THERAPY

CLINICAL PSYCHOLOGY

SPEECH-LANGUAGE PATHOLOGY

COLLEGE OF GRADUATE STUDIES

BIOMEDICAL SCIENCES

PUBLIC HEALTH

PRECISION MEDICINE

Glendale Colleges

ARIZONA COLLEGE OF
OSTEOPATHIC MEDICINE

COLLEGE OF PHARMACY, GLENDALE

COLLEGE OF DENTAL MEDICINE - ARIZONA

ARIZONA COLLEGE OF OPTOMETRY

COLLEGE OF VETERINARY MEDICINE

COLLEGE OF HEALTH SCIENCES

PHYSICIAN ASSISTANT

PHYSICAL THERAPY

OCCUPATIONAL THERAPY

NURSE ANESTHESIA

GRADUATE NURSING

CARDIOVASCULAR SCIENCE

CLINICAL PSYCHOLOGY

SPEECH-LANGUAGE PATHOLOGY

ARIZONA COLLEGE OF
PODIATRIC MEDICINE

COLLEGE OF GRADUATE STUDIES

BIOMEDICAL SCIENCES

PUBLIC HEALTH

PRECISION MEDICINE