



Research: Impacting and Expanding Knowledge

2024

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Message from the President



Dear Faculty and Friends of Midwestern University,

The impact of our faculty and staff in advancing health and well-being is extensive and widespread throughout our communities. Our annual report highlights the commitment of Midwestern University and its faculty to significantly enhance the experiential education of our healthcare students through their work in laboratories and the community.

Under the leadership of Dr. James Woods, Assistant Vice President of Research, we have assembled a support team to assist our faculty and research staff in seeking new funding sources, refining their grants, and guiding them throughout the process. The results of this team's effort are evident in the extensive list of studies found on pages 5-7 of this report.

Research at Midwestern University is improving lives. The project summaries provide a look into how clinical research can be translated from the laboratory to the dental chair, the doctor's office, and to classrooms around the country.

I am proud of the faculty and their accomplishments. Their commitment to teaching the next generation of healthcare providers while inspiring them to expand their intellectual abilities to new and evolving technologies and opportunities is to be celebrated.

Sincerely,

Kathlern H. Cocpringer, Ph.D.

Kathleen H. Goeppinger, Ph.D. President and Chief Executive Officer, Midwestern University

Note to the MWU Community from the Assistant VP of Research



Dear Midwestern University Community,

Over the past year our faculty, staff and students once again demonstrated their ability to significantly advance Midwestern's research programs, particularly when it comes to extramural funding. As I look back at our progress over the last decade, one thing that stands out to me is steady growth. Extramural research expenditures by year is typically the gold standard, which allows institutional comparisons. It was exciting in 2016 to see MWU cross the \$1 million mark for the first time and it is equally exciting to hit a new milestone in 2024 and see us surpass \$5 million in extramural research expenditures!

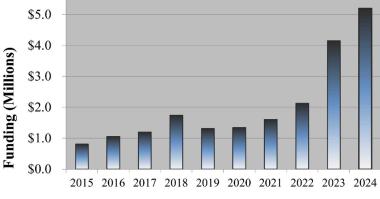
I invite you to read the pages of our annual research booklet to learn a little

more about the research and the individuals that have received some of our extramural funding. You will learn a little about MWU's Computer-Assisted Rehabilitation Environment (CAREN) system, and how this unique biomechanics lab, likely one of the world's most revolutionary environments to study balance and locomotion, is now being used regularly for research. This is followed by two excellent summaries about dental advancements being made at MWU. The first involves training of students who subsequently participate in a practice-based clinical research study. The second describes the use of an engineered natural biomaterial as a potentially much-improved replacement for the currently used dental adhesives for caries. Next, you'll find an overview of how MWU researchers are examining sleep apnea and the

complex pathways which may adapt to lack of oxygen, in efforts to better understand how to direct future clinical trials. Finally, the booklet highlights research providing insights on hospital-acquired pneumonia and how personalized precision dosing of antibiotics can potentially save lives of those with high-risk infections.

All members of our MWU community should be very proud of our research accomplishments!

James M. Woods, Ph.D. Assistant Vice President of Research



MWU Extramural Research Expenditures

Fiscal Year

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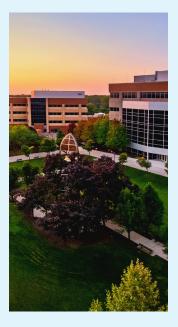
Midwestern University's Commitment to Research

\$5.2 Million

in Extramural Funding Expenditures

in Fiscal Year 2024





\$36.8 Million

Commitment to Research Activities*

in Fiscal Year 2024





* Includes direct and indirect costs. For 2024, this equates to 7.5% of the University budget.

93 Student Research Fellowships

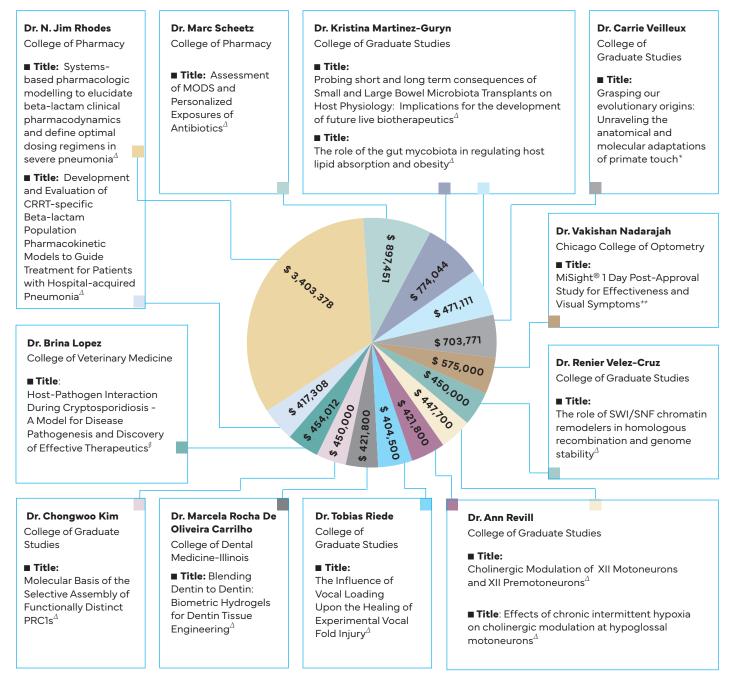
funded at \$525,500

in Fiscal Year 2024





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



Funding sources: [∆]National Institute of Health Awards; *National Science Foundation; [§]USDA National Institute of Food and Agriculture; ⁺⁺CooperVision

Midwestern University Grants Funded from \$100,000 - \$400,000

Investigator/s	College(s	s) Title	Total	Agency
Baab, K.	CGS	Testing Adaptive Hypotheses of Plio-Pleistocene Hominin Craniofacial Evolution	\$330,021	National Science Foundation
Chako, C.	СЛМ	Enhanced Education in Rural Food Animal Practice Dedicated Training for Veterinary Students and Exposure for Native American Youth	\$ 244,491	USDA National Institute of Food and Agriculture
Kreisler, R.	СУМ	The 1000 Canine (1K-9) SARS-CoV-2 Surveillance Study: Exploration of SARS-CoV-2 exposures and transmission pathways among different domestic canine populations	\$121,000	USDA NIFA - Subaward from The Translational Genomics Institute
Molehin, A	CGS	Antigen and adjuvant selection for a vaccine against urogenital schistosomiasis, Hematoshield	\$163,603	National Institutes of Health
O'Neill, M.	CGS	Collaborative Research: The Effects of Musculoskeletal Design on Bipedal Walking and Running Performance in Humans, Chimpanzees and Early Hominins	\$239,935	National Science Foundation
Pais, G.	СОР	Cefepime Physiologically-based Pharmacokinetic Models for Cross-Species Extrapolation	\$ 231,480	National Institutes of Health
Prakapenka, A.	CGS	Alzheimer's disease Pathogenesis in Mothers: A Role for Age and Menopause	\$ 249,946	Alzheimer's Association
Rice, S.	ссо	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
Rhodes, N. J.	CPDG	Development and validation of CRRT-specific beta-lactam population pharmacokinetic models to guide treatment for patients with hospital-acquired pneumonia	\$ 399,991	Food and Drug Administration
Riede, T.	CGS	The Role of Vocal Ligament in Fundamental Frequency and Adduction Control	\$192,212	NIH-R01 Subcontract from the University of Utah
Scheetz, M.	СОР	Evaluating the Temporal Mechanism of Vancomycin Kidney Toxicity as a Means to Prevent Injury	\$ 358,876	National Institutes of Health
Scheetz, M.	СОР	A Randomized Clinical Trial of Continuous vs. Intermittent Infusion Vancomycin: Effects on Measured GFR and Kidney Injury Biomarkers	\$ 119,604	National Institutes of Health
Townsend, K.E.B.	CGS	Collaborative Research: After the Bridgerian Crash - An Integrated Analysis of Mammalian Paleocommunities and Paleoecologies During the Middle Eocene	\$239,596	National Science Foundation
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

Grants Driving Change in Education, Communities



The following grants focus on fostering community outreach and student education through the establishment of training programs for various healthcare professionals while encouraging student research.





Dr. Schea Fissel College of Health Sciences, Glendale Campus Speech-Language Pathology Program

Translational Adapted Groups: Community Builds Capacity for School SLPs

Department of Education **\$1,274,578**

Creates a training program to prepare speech-language pathology students who identify as neurodivergent, bilingual, or BIPOC to serve autistic schoolchildren.



Dr. Lisa Mahaffey College of Health Sciences, Downers Grove Campus Occupational Therapy Program

Tiered Occupational Therapy (TOT): Preparing OT Scholars to Serve on Mental Health Teams

Department of Education **\$1,148,134**

Helps establish a training program for occupational therapists to prepare for service on school mental health teams.

Research Facilities Spotlight



Advancing Rehabilitation and Research: The CAREN at the Midwestern University Therapy Institute

Midwestern University's Glendale Campus is home to a cutting-edge resource that is revolutionizing both rehabilitation and research: the CAREN (Computer-Assisted Rehabilitation Environment) system. This advanced virtual reality platform is one of fewer than 20 in the U.S. and just 50 worldwide, offering a unique combination of immersive environments and precise data collection. Located at the University's Therapy Institute, the CAREN system is a vital tool for Midwestern's faculty healthcare

providers and researchers, enabling a deeper understanding of human movement, balance, and rehabilitation.

The CAREN system is equipped with a moving platform, dual-belt instrumented treadmill, wrap-around projection screens, and a motion capture system, allowing it to simulate realistic environments—from walking through nature to navigating a speedboat on water. This controlled setup provides valuable data on the forces and movements involved in physical activity.

The CAREN system has been utilized in research studies across several programs at Midwestern University, including Optometry, Physical Therapy, Speech-Language Pathology, Podiatry, and Graduate Studies. There are currently seven active faculty-led projects underway using the CAREN, which explore topics ranging from biomechanics and the effects of traumatic brain injury to innovative approaches to rehabilitation.

For Matthew O'Neill, Ph.D. (CGS-Glendale), Associate Professor, Anatomy, the CAREN system is a game-changing tool for his research on musculoskeletal biomechanics. Dr. O'Neill's lab uses the system to investigate how bones, muscles, and the brain work together to enable activities like walking and running. By integrating experimental measurements with computational models, his team is exploring fundamental questions about human locomotion. "The CAREN system is an incredible resource for the type of high-fidelity, integrated biomechanics data collection that is required for my lab's research program," Dr. O'Neill explains. "It allows us to answer a wide range of questions about the musculoskeletal system, from 'how does it work?' to 'when and why did it start to work that way?'"

Dr. O'Neill's work, funded by the National Science Foundation, is led by MWU-based postdoctoral fellow Alicia Blasi-Toccacceli, Ph.D. Their research not only advances basic science but also offers opportunities for students to participate in groundbreaking studies. The data collected through the CAREN system is helping to shed light on how the body's musculoskeletal structures, such as hip joint ligaments and the lower back, influence our movement patterns.

Similarly, Melanie Violand, D.P.M. (AZCPM), Associate Dean, has leveraged the CAREN system to study the effects of total contact casts (TCC) on patients' gait. TCCs are often used to offload pressure from the feet, but they can create a change



in limb length, which impacts the gait of the contralateral limb. Dr. Violand's research, which involves 30 subjects, investigates how these changes in gait can be mitigated with the use of heel and shoe lifts. "The CAREN system significantly streamlined the research process by efficiently collecting data related to speed, single support time, stride length, and ground reaction forces," Dr. Violand notes. Her findings suggest that a heel lift can effectively reduce pressure on the contralateral limb, improving patient outcomes.

The ability to generate high-fidelity data in real time is what makes the CAREN system such a valuable asset to both clinical care and research. Thanks to its versatility in helping assess and treat a wide range of conditions, from neurological disorders to balance and gait issues, while providing researchers with the precise data needed to explore complex questions about human movement, the CAREN is playing a pivotal role in advancing research and student training in the fields of biomechanics, rehabilitation, and clinical care at Midwestern University.



Bridging Oral Health and GI Health While Training Tomorrow's Dental Professionals

"It may be possible to develop a simple gastrointestinal risk assessment based on the information that dental practitioners already obtain during routine dental visits." **Project:** Oral Inflammation and Functional Gastrointestinal Disorders: A Practice-Based Research Approach

Principal Investigators: John C. Mitchell, Ph.D., Associate Dean, College of Dental Medicine-Arizona

Gina Agostini-Walesch, Ph.D., Research Assistant Professor, College of Dental Medicine-Arizona

Co-Investigators: Preetha Kanjirath, B.D.S., M.D.S., M.S., Professor, College of Dental Medicine-Illinois

David Meltzer, M.D., Ph.D., Assistant Dean for Clinical Science Research, Translational, University of Chicago Center for Health and the Social Sciences

Eric Pamer, M.D., Professor of Microbiology and Pathology, University of Chicago

Eugene Chang, M.D., Professor of Medicine, University of Chicago

Mark Lingen, D.D.S., Ph.D., Professor of Pathology and Medicine, University of Chicago

Grant: \$3,417,794 (\$993,973 subaward to University of Chicago) NIH/National Institute of Dental and Craniofacial Research

Dates: 9/13/2023 to 6/30/2028

Midwestern University received a five-year, \$3.4 million grant from the NIH NIDCR PRIMED initiative to establish a sustainable, practice-based clinical research program for dental students and faculty on its Arizona and Illinois campuses. Partnering with the University of Chicago Center for Health and the Social Sciences (UC CHESS), the program offers comprehensive clinical research training and mentoring, including courses, seminars, and handson experience.

In its first year, 37 students and 11 faculty completed the training program, preparing them to begin the first phase of a multi-site clinical study in September 2024. The second site of the clinical study launched in January 2025. Meanwhile, a second cohort of 25 students and four faculty is midway through their training and will join the clinical study in June 2025.

"This award enables us to train students in a practice-based clinical research model, which prepares them to apply information routinely obtained in their clinical practice. We have established a well-organized clinical research infrastructure to answer community-based healthcare questions," says Dr. Mitchell. "Our graduates will play a more active role in producing high-quality research applicable to their patients. We anticipate this research model will reveal relationships between oral and systemic health, leading to improved patient care and more effective dentists."

The program's flagship research project focuses on the link between oral inflammation and

gastrointestinal (GI) disorders, such as IBD, ulcerative colitis, and Crohn's disease. It aims to determine whether symptoms like gum tissue recession or bleeding can predict GI disorders, potentially paving the way for risk assessments during standard dental visits.

Designed to integrate seamlessly into routine dental hygiene visits, the study provides dental students with real-world experience in participant recruitment, data collection, analysis, and reporting. The program allows the students to carry their research training into private practice by building a practical research model while contributing to more diverse and representative clinical research.

An additional facet of this project is that it is collecting data at two distinct academic dental centers. The patient populations in each reflect the diversity of Arizona and Illinois, combining to give a richer cross-section of patient data that is more broadly applicable to the U.S. population than either site individually.

"We are building a clinical research model that is realistic for any clinical environment," says Dr. Agostini-Walesch. "Therefore, another important outcome of our study is that our trained student participants can continue participating in the clinical study activities after they graduate and enter their own private practices."

"This research model will help us recruit the large, naturally diverse samples sorely needed in clinical research—samples that reflect the patient populations seen in average dental practices throughout the United States." Repairing and Regenerating Dentin through Biometric Hydrogels

Project: Blending Dentin to Dentin: Biomimetic Hydrogels for Dentin Tissue Engineering

Principal Investigator: Marcela Rocha de Oliveira Carrilho, D.D.S., Ph.D.

Grant: \$421,800 NIH R15 NIDCR

Dates: 9/7/2023 to 8/31/2026



Marcela Rocha de Oliveira Carrilho, D.D.S., Ph.D., Director of Research, College of Dental Medicine-Illinois (CDMI).

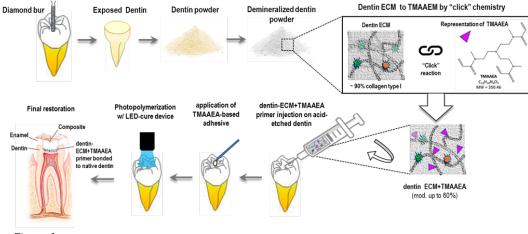


Figure 1: Schematic for design of dentin ECM-derived hydrogel coupled with a triacryamide (TMAAEA) by click chemistry, resulting in a biometric primer for dentin that can be further cross-linked in situ with acid-etched dentin.

Tooth decay figures amongst the most prevalent and consequential oral diseases globally. In the U.S. alone, over 90% of adults, 50% of children between the ages of six to eight years-old, and 60% of adolescents between the ages of 12-19 have experienced dental caries (cavities or tooth decay). Part of the economic burden of untreated dental caries can be counted in terms of indirect costs because of productivity losses due to absenteeism from work and school. Rather than taking a preventative approach, the current model focuses on treating caries sequelae (dental conditions) by filling cavities with tooth-colored restorations based on resin methacrylates (chemicals utilized to create dental materials).

However, despite more than six decades of diligent research by different research groups, including ones at Midwestern University, achieving a durable bond of methacrylate resin-based restorations remains a challenge. In fact, the estimated annual costs nationwide to replace defective resin restorations are around five billion dollars.

"The overall goal of our research is to use an engineered natural biomaterial to solve this problem." said Marcela Rocha de Oliveira Carrilho, D.D.S., Ph.D., Director of Research, College of Dental Medicine-Illinois (CDMI). "We are developing hydrogels that are made of the extracellular matrix (ECM) of demineralized dentin functionalized with acrylamides. We hypothesize that this hybrid material will produce resin dental adhesives that are less vulnerable to undergo hydrolytic degradation (chemical reaction that breaks down polymer bonds), Ultimately, this research is pioneering because it proposes for the first time a dental adhesive that is truly biomimetic to dentin and, as such, will have the ability to not only aid in the repair of dental caries lesions, but also regenerate dentin better than current methacrylate dental adhesives."

⁴⁴ This research is pioneering because it proposes for the first time a dental adhesive that is truly biomimetic to dentin and, as such, will have the ability to not only aid in the repair of dental caries lesions, but also regenerate dentin better than current methacrylate dental adhesives.⁹⁹

"The central goal of this proposal is to develop a biomimetic methacrylate-free dental primer that will restore the function of caries-affected teeth and, at the same time, serve as a scaffold for dentin regeneration," Dr. Rocha de Oliveira Carrilho explained. "Eliminating methacrylates in this novel dental primer is the key to produce more durable bonded interfaces under restorations. We will functionalize dentin ECM from healthy and caries-affected extracted teeth with an acrylamide via thiol-click reaction, creating hydrogels with relatively lower sensitivity to water's hydrolytic effects. Several photo-crosslinkable collagen/gelatin derivatives have emerged over the past decade, including a highly functionalized gel-MA developed in our laboratory," she said. "However, the functionalization of the dentin ECM with acrylamides remains underexplored. Our preliminary studies show that the methacryloyl modification of dentin ECM is a promising route to obtain an injectable biomaterial that can serve as a parent biomaterial for dentin while bonding to both dentin and restorative composites. Thus, the significant contribution of this study will be to develop hybrid hydrogels that combine insoluble and soluble fractions of dentin extracellular matrix with acrylates to produce a biomimetic dental material dedicated in primis for bioengineering of affected teeth (see Figure 1)."



** Exploring how obstructive sleep apnea and intermittent reduced oxygen levels affect the brain's control of the upper airway is crucial for understanding the disease and identifying new treatment options.** **Project:** Effects of chronic intermittent hypoxia on cholinergic modulation at hypoglossal motoneurons

Principal Investigator: Ann L. Revill, Ph.D., College of Graduate Studies, Glendale Campus, Associate Professor, Physiology

Co-investigators: Amanda Melin, Ph.D., Associate Professor of Anthropology and Archaeology, University of Calgary; Magdalena Muchlinski, Ph.D., Professor, Academic Affairs, Oregon Health and Science University

Grant: \$421,800 NIH/NLHBI Grant (R15HL175526) **Dates:** 09/01/2024 to 08/31/2027

Obstructive sleep apnea (OSA) is a common sleep disorder where repeated pauses in breathing cause drops in blood oxygen levels—an effect known as chronic intermittent hypoxia (CIH). These oxygendeprivation episodes can lead to significant changes in the brain, particularly in the neurons responsible for controlling breathing. One major issue in OSA is the reduced activity of tongue muscles, which normally keep the airway open. This reduction is linked to cholinergic neurons—specialized brain cells that release acetylcholine, a chemical messenger crucial for regulating airway tone.

A new research project investigates how CIH impacts the cholinergic system and its connections to hypoglossal motoneurons, which activate the tongue muscles. Using advanced imaging techniques, the study will examine structural changes in the brain, such as alterations in cholinergic receptors on hypoglossal motoneurons and shifts in the density of acetylcholine-releasing neurons. It will also explore functional changes by studying breathing-related activity in isolated brainstem slices, focusing on how CIH affects acetylcholine's role in modulating hypoglossal motoneuron activity. Since the brain's ability to adapt, or its plasticity, changes with age, the study will compare these structural and functional changes in newborn and adult mice to determine how age influences the brain's response to CIH.

The results of this study are expected to provide critical insights into how the cholinergic system adapts—or fails to adapt—to chronic oxygen deprivation. Such findings are particularly important given that many current drug therapies in clinical trial for OSA target the cholinergic system. A deeper



Ann L. Revill, Ph.D., Associate Professor, Physiology, Graduate Studies, Glendale Campus (CGS)

understanding of how this system functions and changes under CIH associated with OSA could pave the way for more effective treatments.

Ann L. Revill, Ph.D., Associate Professor, Physiology, Graduate Studies, Glendale Campus (CGS), the project's lead investigator, highlights the significance of this research, stating, "Exploring how obstructive sleep apnea and reduced oxygen levels affect the brain's control of the upper airway is crucial for understanding the disease and identifying new treatment options. I'm excited to collaborate with Midwestern students to tackle this challenge." Precision Dosing to Combat Hospital-Acquired Pneumonia (HAP) for Improvement of Patient Outcomes

N. Jim Rhodes, Pharm.D., M.S., BCPS, Associate Professor of Pharmacy Practice, College of Pharmacy, Downers Grove (CPDG)

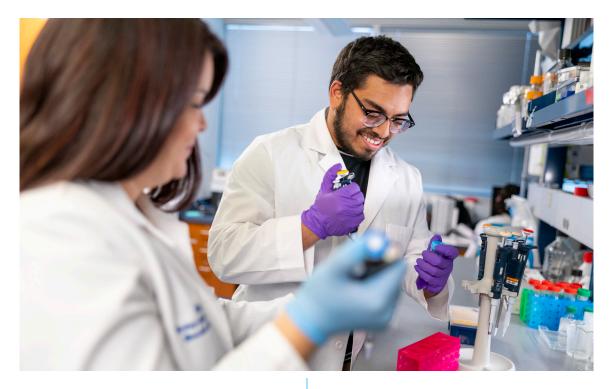
** This research is significant because it tackles an urgent need to improve clinical outcomes among vulnerable patients for whom treatment options are limited and the risk of death from infection is high.

Project: Development and Evaluation of CRRT-specific Beta-lactam Population Pharmacokinetic Models to Guide Treatment for Patients with Hospital-Acquired Pneumonia

Principal Investigator: N. Jim Rhodes, Pharm.D., M.S., BCPS Associate Professor of Pharmacy Practice, College of Pharmacy, Downers Grove (CPDG)

Grant: \$417,308 NIH R21 (NIAID) Prime with Subcontract to Northwestern University

Dates: 6/23/2023 to 5/31/2025



This research focuses on improving the treatment of hospital-acquired pneumonia (HAP), a lifethreatening condition often caused by antibioticresistant bacterial organisms such as Klebsiella pneumoniae and Pseudomonas aeruginosa. Many critically ill patients with HAP do not respond well to antibiotics because typical antibiotic doses are not adequate. More specifically, severe illness and the use of continuous dialysis can lead to changes in antibiotic concentrations, which can increase the risk of overdosing and underdosing. Current antibiotic dosing guidelines are not tailored to the unique needs of these patients. This project aims to develop personalized or "Precision Dosing" models for beta-lactam antibiotics, which are a key treatment for HAP, to ensure that patients receive the right dose to treat their infections.

"This research is significant because it tackles an urgent need to improve clinical outcomes among vulnerable patients for whom treatment options are limited and the risk of death from infection is high. By using advanced computer methods and site-ofinfection sampling from patients with pneumonia, our team will create models to predict how CRRT (continuous renal replacement therapy) affects drug levels in the body and lungs," said N. Jim Rhodes, Pharm.D., M.S., BCPS, Associate Professor of Pharmacy Practice, College of Pharmacy, Downers Grove (CPDG). "We will also develop a web-based calculator to help physicians and pharmacists provide customized dosing for each patient. We plan to validate the tools developed in this study further in subsequent clinical studies."

Midwestern University Tomorrow's Healthcare Team

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Midwestern University Illinois Colleges

555 31st Street | Downers Grove, Illinois 60515

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 Graduate Nursing Programs

College of Graduate Studies Biomedical Sciences | Public Health Precision Medicine

Proposed College of Veterinary Medicine-Illinois

Midwestern University Arizona Colleges

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Arizona College of Osteopathic Medicine College of Pharmacy, Glendale College of Dental Medicine - Arizona Arizona College of Optometry Arizona College of Podiatric Medicine College of Veterinary Medicine College of Veterinary Medicine College of Health Sciences Physician Assistant | Physical Therapy Occupational Therapy | Nurse Anesthesia Programs Cardiovascular Science | Clinical Psychology Speech-Language Pathology | Graduate Nursing Programs College of Graduate Studies Biomedical Sciences | Public Health Precision Medicine







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