



Research: Impacting and Expanding Knowledge

2023

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Downers Grove, Illinois 60515

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Glendale, Arizona 85308

Message from the President



Dear Faculty and Friends of Northwestern University,

The past year was one of very significant accomplishments by our faculty as they expanded their commitment to research as highlighted in this annual report.

The commitment to research activities for the past fiscal year was an all-time high of \$35.4 million dollars, while the extramural funding expenditures was \$4.1 million for the fiscal year. As an academic institution dedicated to the education of the next generation of healthcare professionals, I am proud of the 96 student research fellowships that were funded by the university to expand the experience and commitment of our students to research. These students worked closely with their faculty mentors and many of the Primary Investigators on significant projects that had meaningful impact on their future careers in healthcare.

Many of these students worked in the Core Research Facilities that houses state-of-the-art instrumentation providing a wide range of scientific experiments from all of our faculty. This annual report highlights the work being

done in the Arizona Core Facility that was used over 2,500 times by more than 80 researchers, with half of those researchers being students. It is our goal that introducing our students to the opportunities to do scientific inquiry while they are at Northwestern University will encourage them to continue this search for innovative solutions in disease management and new knowledge that can bridge the gap between past healthcare practices to more effective ways to provide patient care.

At Northwestern University we seek to stimulate a commitment to research in all our professions. We take great pride in the research outcomes, the many publications and scientific presentations, and the impact research has on the well-being of our communities. Please join me in congratulating all of our faculty that have been honored in this year's Annual Research Report. Their work and commitment to our students is a testament of their dedication to our mission.

Sincerely,

Kathleen H. Goepfinger, Ph.D.

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



Dear MWU Community,

It's an exciting time to watch Midwestern University's research enterprise continue to emerge and develop. Not only do we have outstanding faculty members who educate the healthcare workforce of tomorrow in the classroom, but they also contribute to the advancement of knowledge through research. I've always been of the belief that teaching and research go hand in hand. As a student, it always stood out to me when a professor could teach a subject and reference findings or provide examples from their own research lab, demonstrating that they're at the forefront of their field. I also found it particularly insightful when they could state that which was generally known or accepted, what was currently being researched or questioned, and what was not known. This practice of questioning what we and others believe about how a process works, testing it systematically,

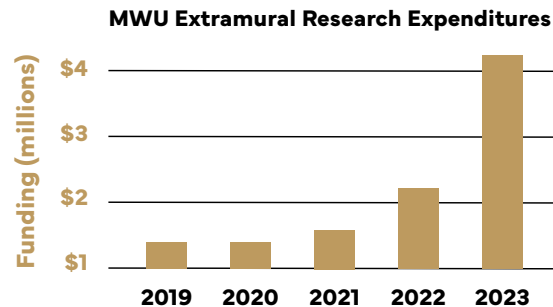
and then either confirming it or coming to a new realization which can also be tested and proven, is such a necessary practice at a time when disinformation can so easily be spread. I'm incredibly proud of our Midwestern faculty members who consistently contribute to the research process in a manner that significantly improves human and animal health.

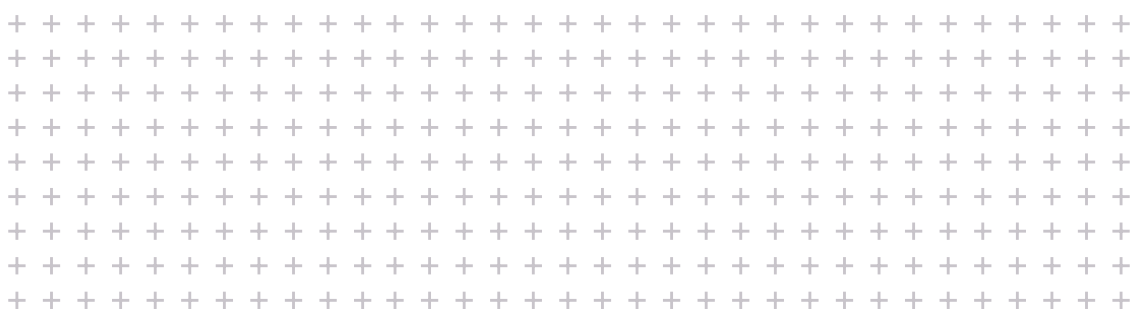
In calendar year 2023, Midwestern had 17 active grants funded at \$400,000 or more, where 14 of these (82%) could broadly be characterized as research-focused grants (page 5). The remaining three sponsored programs (page 7) each have a significant training component, not to mention very laudable goals, where some also include a research component. In the four years that we've been preparing research booklets based on the calendar year, these numbers have steadily trended upwards. In 2020 we had 7 active awards >\$400,000 and that increased to 17 in 2023. This increase in awards is also starting to be noticeable in Midwestern's annual extramural research expenditures, which is a number that we provide annually through surveys to the National Science Foundation and the National Institutes of Health.

MWU researchers should be very proud!

Sincerely,

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





Research: Impacting and Expanding Knowledge

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Midwestern University's Commitment to Research

MWU

\$35.4 Million

**Commitment to
Research Activities***

in Fiscal Year 2023



\$4.1 Million

**in Extramural
Funding
Expenditures**

in Fiscal Year 2023

**96 Student
Research
Fellowships**

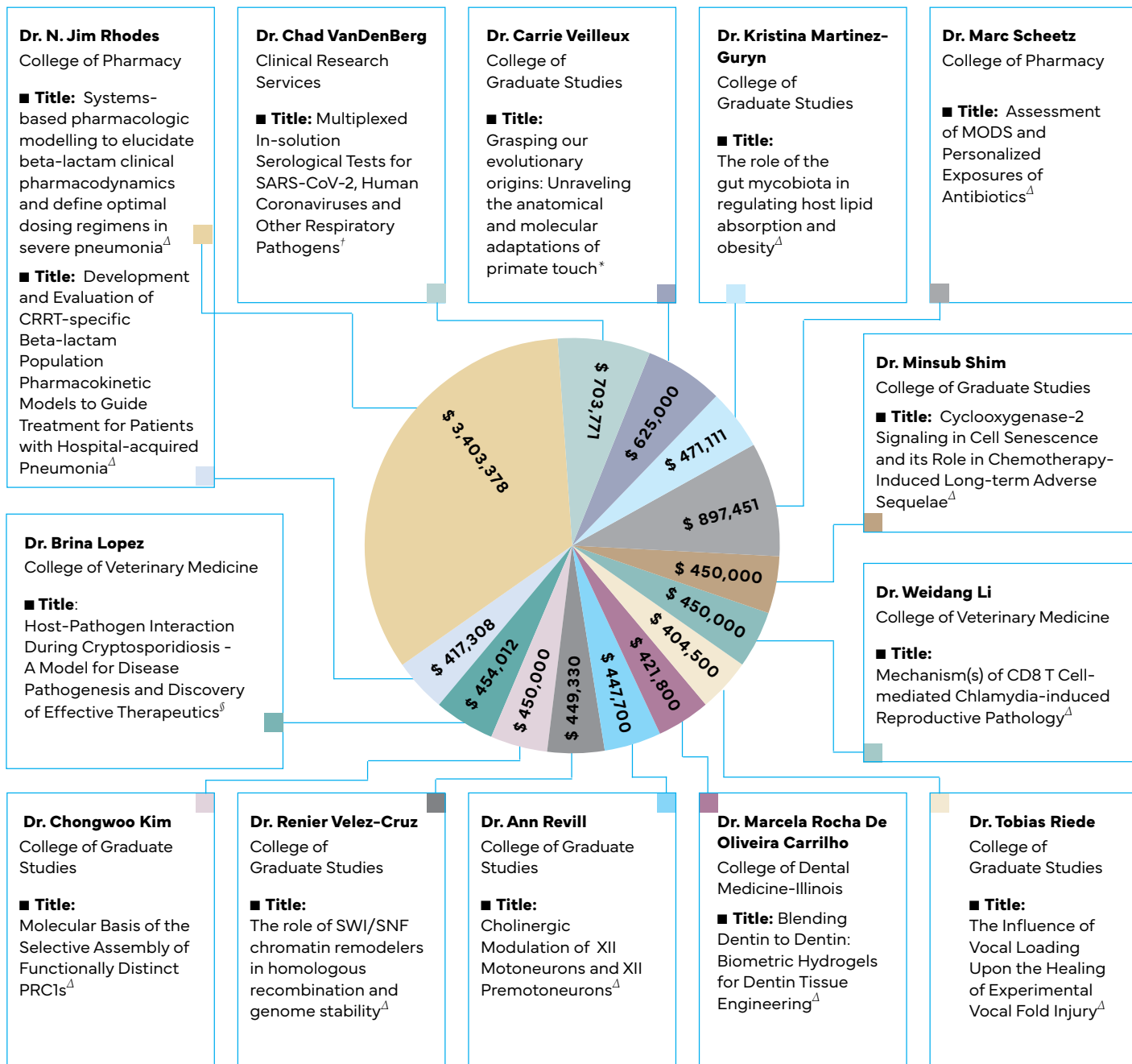
funded at
\$433,500

in Fiscal Year 2023



**Includes direct and indirect costs.
For 2023, this equates to 7.5%
of the University budget.*

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



Funding sources: ^ΔNational Institute of Health Awards; [§]USDA National Institute of Food and Agriculture; [†]Leidos/ASU/NIH; ^{*}National Science Foundation

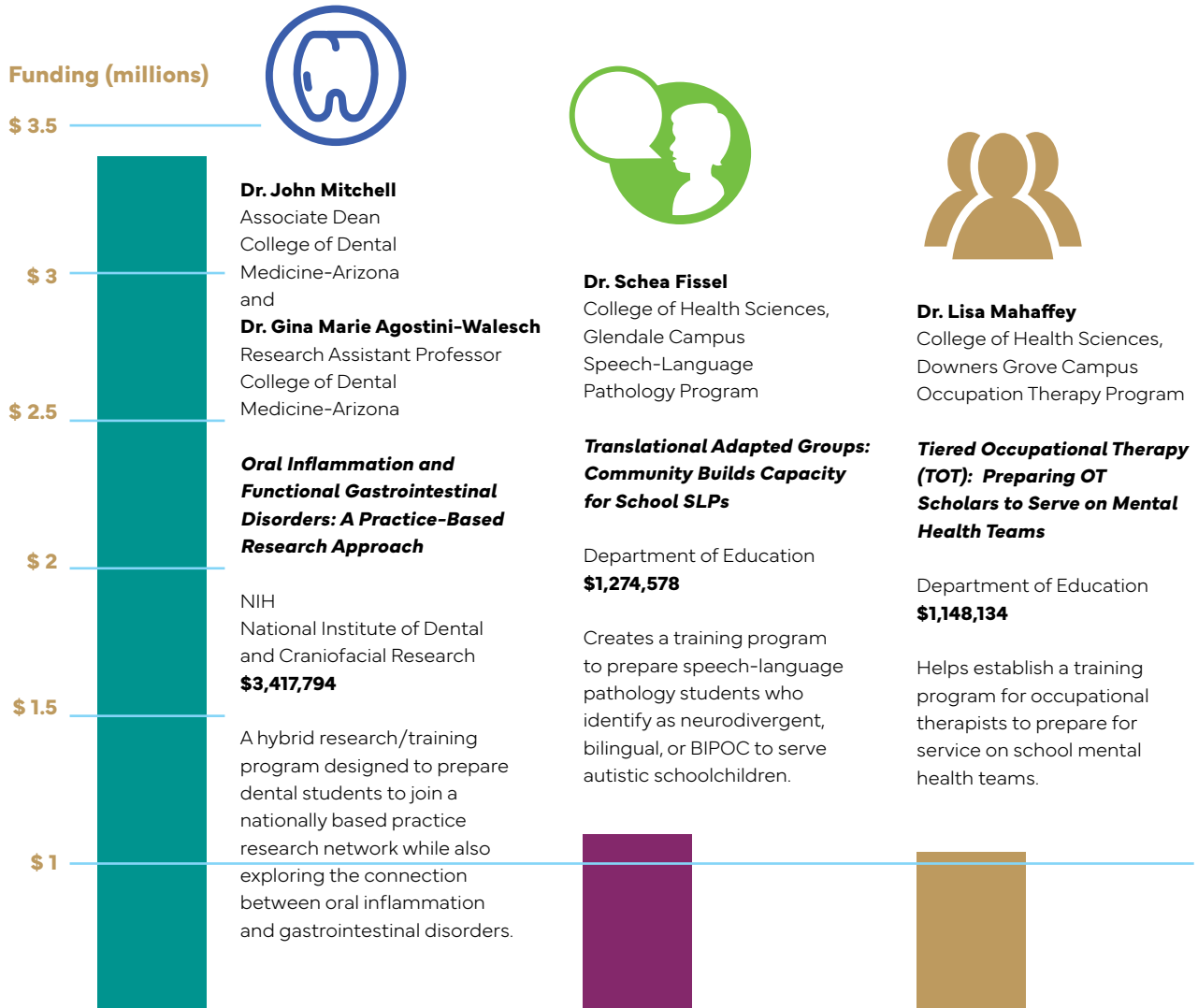
Midwestern University Grants Funded from \$100,000 – \$400,000

Investigator/s	College(s)	Title	Total	Agency
Baab, K.	CGS	Testing Adaptive Hypotheses of Plio-Pleistocene Hominin Craniofacial Evolution	\$ 330,021	National Science Foundation
Chako, C.	VVM	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
Elbayoumi, T. and Yao, M.	COP	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
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.	COP	Cefepime Physiologically-based Pharmacokinetic Models for Cross-Species Extrapolation	\$ 231,480	National Institute of Health
Prakapenka, A.	CGS	Alzheimer's disease Pathogenesis in Mothers: A Role for Age and Menopause	\$ 249,946	Alzheimer's Association
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
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
Riede, T.	CGS	Collaborative Research: Evolution of Long-distance Communication in Vocal Rodents	\$193,774	National Science Foundation
Scheetz, M.	COP	Evaluating the Temporal Mechanism of Vancomycin Kidney Toxicity as a Means to Prevent Injury	\$ 358,876	National Institute of Health
Scheetz, M.	COP	A Randomized Clinical Trial of Continuous vs. Intermittent Infusion Vancomycin: Effects on Measured GFR and Kidney Injury Biomarkers	\$ 119,604	National Institute of Health
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
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

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 and encourage student research.



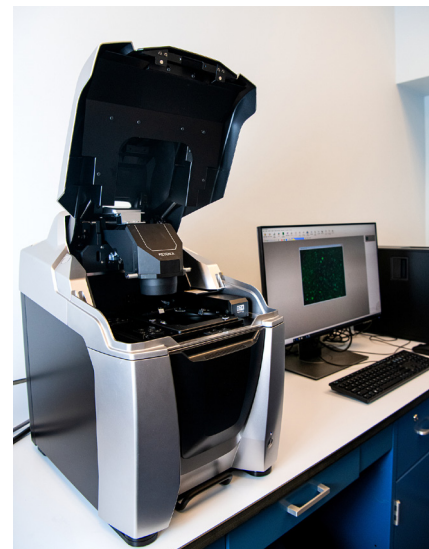
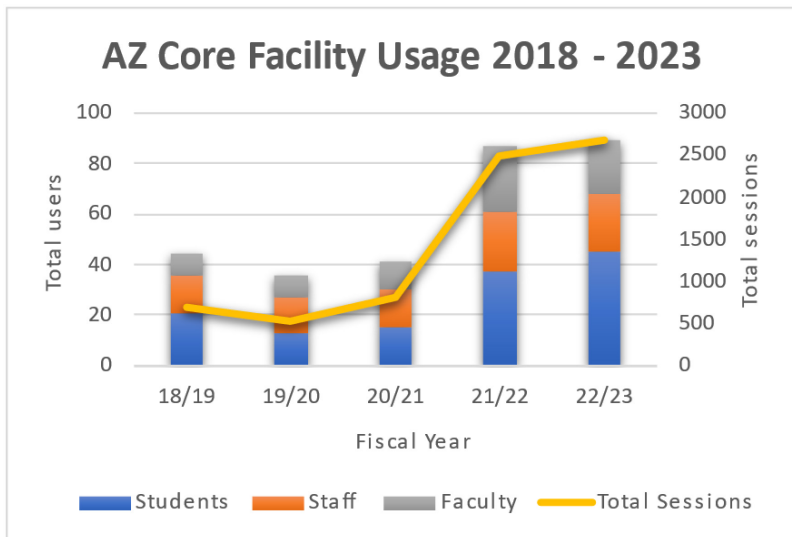


AZ-Core Facility Keeps Midwestern Researchers on the Cutting Edge

*Manan Damani,
Research
Specialist,
Glendale Core
Facility*

The mission of the AZ Core Facility is to provide access to shared research equipment and acquire new technologies that are out of reach to individual investigators or academic units. It is actively funded by Midwestern University to maintain existing instruments and to add new equipment and resources. The AZ Core Facility has dedicated rooms in the Foothills Science Center and Cactus Wren Hall for Cell & Analytical Biology, Cell & Tissue Culture, Histology, Microscopy, and Image Processing.

Unlike other core facilities, the AZ Core Facility generally operates as a “free-of-charge” center. Most instruments are available on a direct walk-up basis. That means that once users are trained, they may reserve time on instruments using the University’s online scheduling system. The record of users includes faculty, staff, and students.

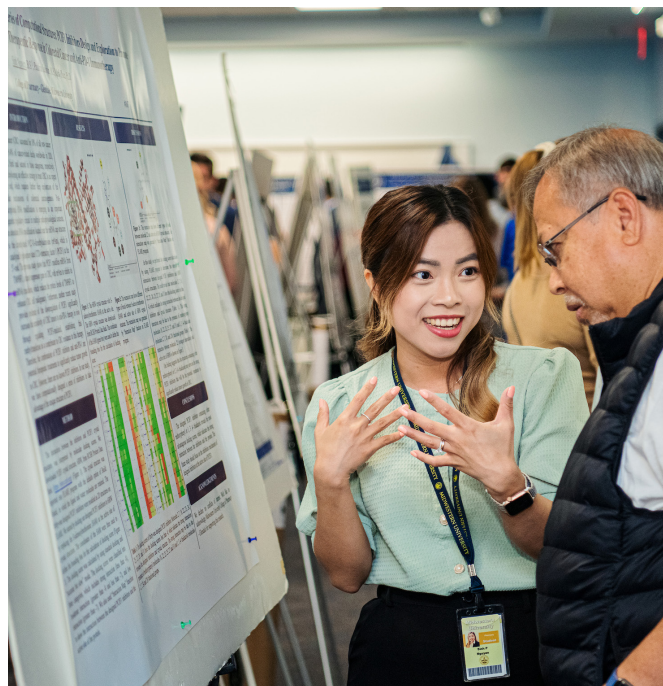


The AZ Core Facility houses research equipment in several rooms, but the headquarters is located in Foothills Science Center 126. It is overseen by faculty advisor Andrew Lee, Ph.D., Professor, Anatomy, and managed by a full-time Research Specialist, Manan Damani. Manan trains users, provides troubleshooting, and assists in assessing the research needs of the Midwestern University community.

Over the past five years, the AZ-Core Facility has seen a doubling in the number of users and quintupling of usage (as measured by session count), with significant increases in microscopy, histology, and 3D imaging.

For more information about the AZ-Core Facility, visit:

<https://www.midwestern.edu/research/glendale-core-research-facility>.



Renier Vélez-Cruz, Ph.D., Associate Professor, Biochemistry and Molecular Genetics, Midwestern University, College of Graduate Studies, Downers Grove

Identifying Specific Subunits of the SWI/SNF Chromatin Remodeler for Targeted Chemotherapy

“ In the near future, this work will become more relevant, as precision medicine approaches will become standard, and we will know that a particular cancer type bearing a specific mutation has a specific DNA repair defect and will respond better to a particular type of chemotherapy.”



Project: The role of SWI/SNF chromatin remodelers in homologous recombination and genome stability

Principal Investigator: Renier Vélez-Cruz, Ph.D., Associate Professor, Biochemistry and Molecular Genetics, Midwestern University, College of Graduate Studies, Downers Grove

Grant: \$449,330 NIH (NCI - R15)

Dates: 8/10/22 to 7/31/2025

Project Summary:

Cancer is the second leading cause of death in the United States, close behind heart disease. It is therefore critical to continue our work towards the improvement of cancer therapies. Radiation therapy and the vast majority of chemotherapeutic agents currently in use to treat cancer work by damaging the cancer cell's DNA, thus killing the tumor. The damage caused by these drugs is repaired by various DNA repair pathways, such as homologous recombination repair (HRR). Tumors bearing mutations in genes that are important for HRR become more sensitive to these chemotherapeutic agents, such as breast and ovarian cancers carrying mutations in the BRCA1 or BRCA2 genes. Moreover, researchers have identified drugs known as PARP (Poly ADP ribose polymerase) inhibitors that target specifically HRR-deficient cancer.

Renier Vélez-Cruz is an Associate Professor in the Department of Biochemistry and Molecular Genetics on the Downers Grove Campus with a long-standing interest in DNA repair and the improvement of cancer therapies. Dr. Vélez-Cruz's lab identified a role for a group of large molecular complexes known as SWI/SNF chromatin remodelers in the repair of DNA double-strand breaks (DSBs) through the HRR pathway. These complexes are composed of 10-15 subunits and are responsible for pushing and sliding nucleosomes along the DNA, thus changing chromatin structure by either increasing or decreasing DNA accessibility. SWI/SNF complexes had an established role in transcription regulation, but more recent work has identified a role for these complexes in DNA repair. Dr. Vélez-Cruz's laboratory published a study showing that inactivation of the main catalytic

subunit of these complexes, known as BRG1, plays a role in HRR and loss of this gene results in cancer cells that are sensitive to a variety of chemotherapeutic drugs. The importance of this work is underscored by the fact that multiple subunits within the SWI/SNF chromatin remodeling complexes are mutated in up to 20% of human cancers.

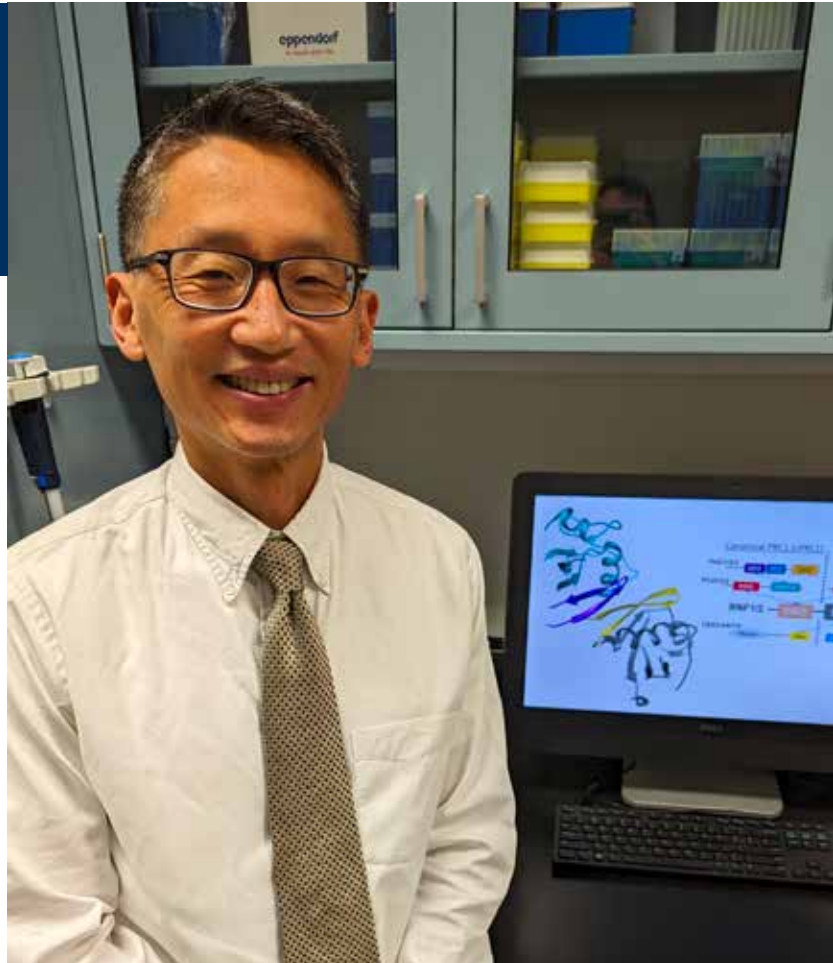
"We have various aims in this proposal. First, we intend to identify the SWI/SNF subunits that are required for the function of these complexes in HRR. Second, we intend to test whether the catalytic activity of the main ATPases (proteins) of these complexes are good targets for cancer therapy. Third, we will test whether inactivation of various SWI/SNF subunits renders cancer cells sensitive to various chemotherapeutic drugs, including PARP inhibitors" said Dr. Vélez-Cruz regarding his funded award from the National Cancer Institute (NCI).

By identifying the SWI/SNF subunits required for this DNA repair function, Dr. Vélez-Cruz and his team are also identifying DNA repair vulnerabilities in these cancers that can be exploited therapeutically. These studies are also shedding light on the function of these complexes in HRR, and the HRR process itself. In the near future, this work will become more relevant, as precision medicine approaches will become standard, and we will know that a particular cancer type bearing a specific mutation has a specific DNA repair vulnerability and will respond better to a particular type of chemotherapy," he said.

Piecing Together the Polycomb Group Protein Puzzle

Chongwoo A. Kim, Ph.D.,
Professor, Biochemistry and
Molecular Genetics, College of
Graduate Studies, Glendale

“Over the last 20 years, a series of 1:1 protein-protein interactions have been identified for PRC1, but the larger picture remains unresolved.”



Project: Molecular Basis of the Selective Assembly of Functionally Distinct PRC1s

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

Grant: \$450,000 NIH-R15

Dates: 9/22/2022 to 8/31/2025

Project Summary:

The Polycomb group (PcG) is a family of proteins that, among its many functions, maintains how stem cells function and are also important indicators of cancer development, as overexpression of PcG proteins correlates with the severity and invasiveness of several cancer types. The PcG functions by having multiple proteins bind and work together. In 1999, the first PcG complex was isolated from fruit flies (*Drosophila*) containing four members and was aptly named Polycomb Repressive Complex 1 (PRC1). In the human version, PRC1 is categorized as either canonical (cPRC1), for those housing the same four core member proteins as the fruit fly version, or variant (vPRC1), for those that have diversified its membership. Knowing how PRC1 is assembled, or how the pieces of the PRC1 jigsaw puzzle are arranged, would be important to help understand this important system. Over the last 20 years, a series of 1:1 protein-protein interactions, or two pieces of the puzzle, have been identified for PRC1 proteins, but the larger picture remains unresolved.

“We hypothesize that cPRC1 assembles in a manner where two connected pieces of the puzzle can interact with a different two-piece combination of the puzzle,” Dr. Kim said. “These ‘secondary’ protein-protein interactions within cPRC1 underlie the reason for how PRC1 separately assembles c- and vPRC1 and creates multiple cPRC1s with diversified functions. We intend to investigate the molecular mechanisms that determine this assembly. In other words, complete the cPRC1 jigsaw puzzle and view what the final picture looks like.”

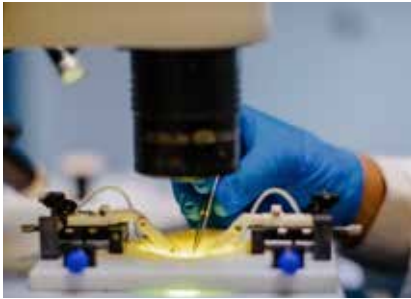
By defining the molecular choreography underlying PRC1 assembly, Dr. Kim hopes to provide a new perspective on the regulation and function of these complexes in genome regulation. The study’s results may also be broadly applicable for understanding other gene regulatory systems, many of which utilize multiple pieces whose arrangement in the larger picture has not yet been defined.



■ Mapping the Secrets of Precision Touch



“ Precision touch, which allows us to discern texture, shape, and movement, is particularly crucial for human and primate sensory biology and health. ”



Carrie C. Veilleux, Ph.D.,
Assistant Professor, Anatomy,
College of Graduate Studies, Glendale

Project: Unraveling the anatomical and molecular adaptations of primate touch

Principal Investigator: Carrie C. Veilleux, Ph.D., Assistant Professor, Anatomy, College of Graduate Studies, Glendale

Co-investigators: 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: \$625,000 NSF

Dates: 9/01/2022 to 8/31/2027

Project Summary:

Touch sensation is a fundamental aspect of how humans and animals interact with their environment. Precision touch, which allows us to discern texture, shape, and movement, is particularly crucial for human and primate sensory biology and health. Highly sensitive precision touch in human fingers, for example, is what allows us to check fruit ripeness or engage in fine motor manipulation and tool use. However, the factors influencing the evolution of precision touch remain largely unexplored.

This project embarks on an in-depth investigation into the genetics, anatomy, and behavior of how precision touch varies across diverse array of primates and other mammals. It is structured around three key questions: (1) what genes impact variation in precision touch receptors in the skin? (2) how does dietary strategy, tool use, and arboreality affect adaptations for precision touch? (3) do primates and humans have more sensitive precision touch in the hands than other mammals? To investigate these questions, the researchers are collaborating with veterinarians at wildlife sanctuaries in Costa Rica and captive facilities in the United States to build a biobank of tissues, sampling from 11 body regions of at least 18 different species, many of which are endangered or understudied. Beyond advancing scientific knowledge, the project will enhance public awareness of sensory systems through an interactive exhibit at the Arizona Museum of Natural History and foster STEM research training for undergraduate and graduate students across the United States, Canada, and Costa Rica.

By employing a multidisciplinary approach that includes transcriptome sequencing, histology, and morphometrics, this project is poised to significantly

advance understanding of precision touch and its role in mammal sensory ecology and evolutionary theory.

“The array of samples we’re collecting for this project is pretty unprecedented. Our understanding of touch across mammals has been historically limited to common lab models or specialized animals like the star-nosed mole. Through this project, we’re able to explore precision touch across wild primates, sloths, raccoons, coatis, kinkajous, anteaters, possums, agoutis, squirrels ... and I really hope that Midwestern students will want to dive in and help study these awesome animals,” Dr. Veilleux said.



Marc Scheetz, Pharm.D., M.Sc, Associate Dean of Research,
College of Pharmacy, Professor, and Director of the Pharmacometrics
Center of Excellence, Midwestern University, Downers Grove

■ Attaining Precision Antibiotic Doses for Children with MODS



“ Timely attainment of target antibiotic concentrations is a crucially important, modifiable intervention to increase survival in these children, yet we currently have limited data on antibiotic pharmacokinetics (PK) in children with MODS with which to develop personalized dosing strategies. ”

Project: Assessment of MODS and Personalized Exposures of Antibiotics

Principal Investigator: Marc Scheetz, Pharm.D., M.Sc, Associate Dean of Research, College of Pharmacy, Professor, and Director of the Pharmacometrics Center of Excellence, Midwestern University, Downers Grove

Grant: \$897,451 NIH

Dates: 9/22/2021 to 8/31/2026

Project Summary:

Multiple Organ Dysfunction Syndrome (MODS) affects as many as 57% of critically ill children, with mortality rates as high as 67% in those infected. The long-term goal of this proposal, Antibiotics in MODS: Personalizing Exposures (AMPLE), is to leverage the well-established infrastructure from an ongoing clinical trial to identify optimal antibiotic dosing strategies for this highly understudied, high-risk population.

Infection is a common occurrence in children with MODS, either as an inciting insult or a result of a new, nosocomial infection. However, management of children with MODS and infection is complicated by the development of immune paralysis (IP), which has deleterious effects on immune function. Unfortunately, antibiotic management strategies and how they should be modified as a function of host immune status are key knowledge gaps in pediatric MODS. Timely attainment of target antibiotic concentrations is a crucially important, modifiable intervention to increase survival in these children, yet researchers currently have limited data on antibiotic pharmacokinetics (PK) in children with MODS with which to develop personalized dosing strategies. "We will quantify antibiotic PK in 400 subjects from a 22-center, prospective study of the epidemiology and risk factors for IP in 1400 children with MODS. The objectives of this application are to use samples and clinical data to characterize the variability of concentrations for the antibiotics most commonly used in pediatric MODS; to investigate the relationships between antibiotic target attainment and outcomes in pediatric MODS with and without IP; and to develop model-based dosing approaches that rapidly achieve and maintain target antibiotic concentrations. The central hypothesis of this proposal is that

precision, PK-driven antibiotic dosing strategies can be developed that adequately account for organ dysfunction and immune function in children with MODS," Dr. Scheetz said.

Dr. Scheetz will work with his Co-Principal Investigator, Dr. Kevin Downes, to lead a team of researchers to pursue the following aims:

- To create and evaluate sophisticated population PK models for the six most commonly used antibiotics in pediatric MODS.
- To define antibiotic target windows outside of which children with MODS (with and without immunoparalysis) who are being treated for infection are at increased risk for death and prolonged organ failure.
- To use simulations to identify dosing strategies that achieve and maintain antibiotic concentrations within defined therapeutic windows.

The proposed studies will answer the following key questions about the pharmacology of pediatric MODS:

- What proportion of children are underexposed or overexposed using the current standard dosing approaches?
- How does MODS impact antibiotic PK and outcomes in children?
- How does IP impact necessary target concentrations in pediatric MODS?

"We expect this research to result in first-of-its-kind data that are crucial toward developing Precision Antibiotic Dosing strategies for children with MODS," Dr. Scheetz added.



Midwestern University

Tomorrow's Healthcare Team

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Midwestern University Illinois Colleges

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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

Midwestern University Arizona Colleges

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College of Dental Medicine - Arizona

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