

ROUNDING WITH THE DEANS OF THE SCHOOL OF MEDICINE

Rounding with Joseph E. Kerschner, MD

Provost and Executive Vice President, The Julia A. Uihlein, Dean of the School of Medicine
and

Deborah Costakos, MD, MS, Interim Dean Designate School of Medicine, Professor and Chair, R.D. and Linda
Peters Professor in Ophthalmology

Knowledge changing life in the Department of Biophysics

On Tuesday, November 26, 2024, Deborah Costakos, MD, MS, Interim Dean Designate School of Medicine, Professor and Chair, R.D. and Linda Peters Professor in Ophthalmology, Department of Ophthalmology & Visual Sciences, and I rounded in the Department of Biophysics. Francesca M. Marassi, PhD, Eminent Scholar, Professor and Chair in the Department of Biophysics, and her team hosted a welcoming and engaging visit.

The team shared that research in the Department of Biophysics centers around three themes: imaging-guided therapeutic development, structural biology, and redox biology and drug development.

We first heard about using imaging-guided therapeutic developments for treating glioblastoma. The team working on imaging-guided therapeutic development includes:

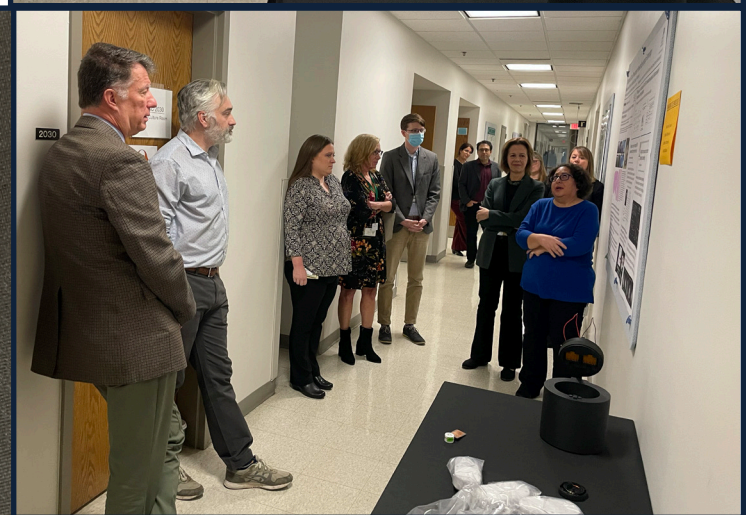
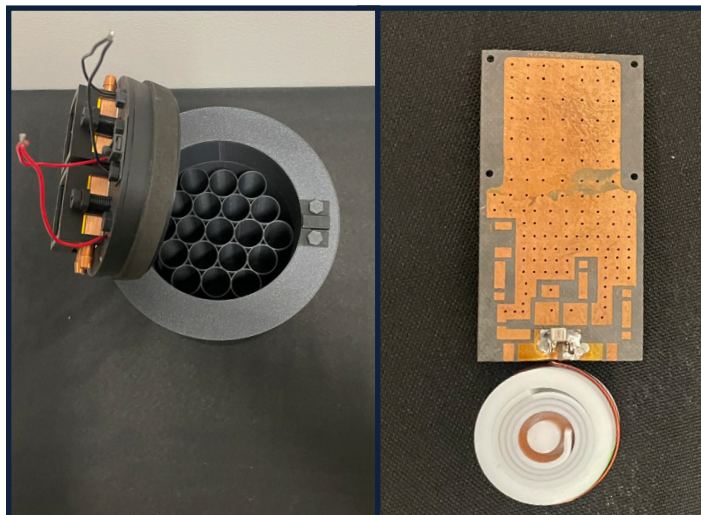
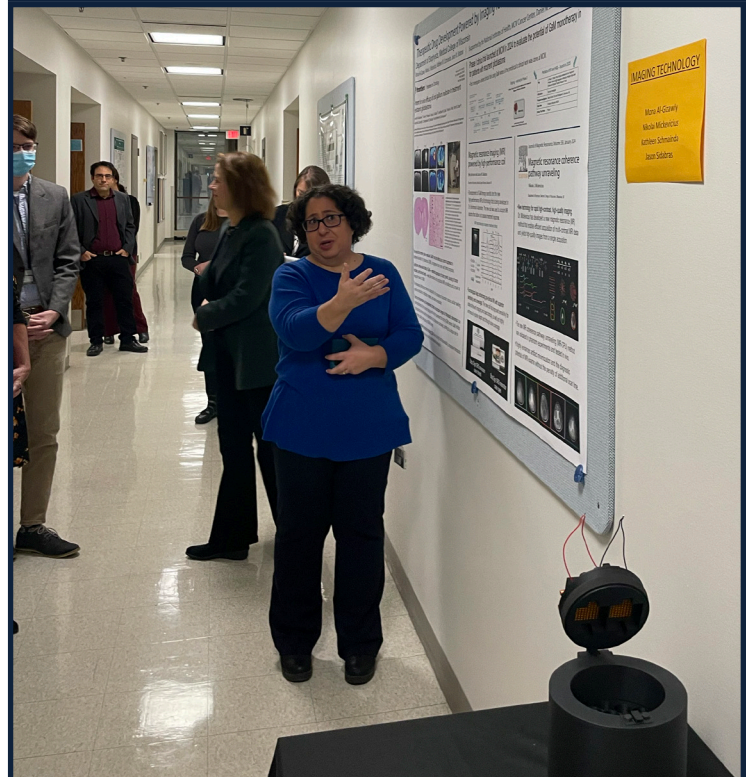
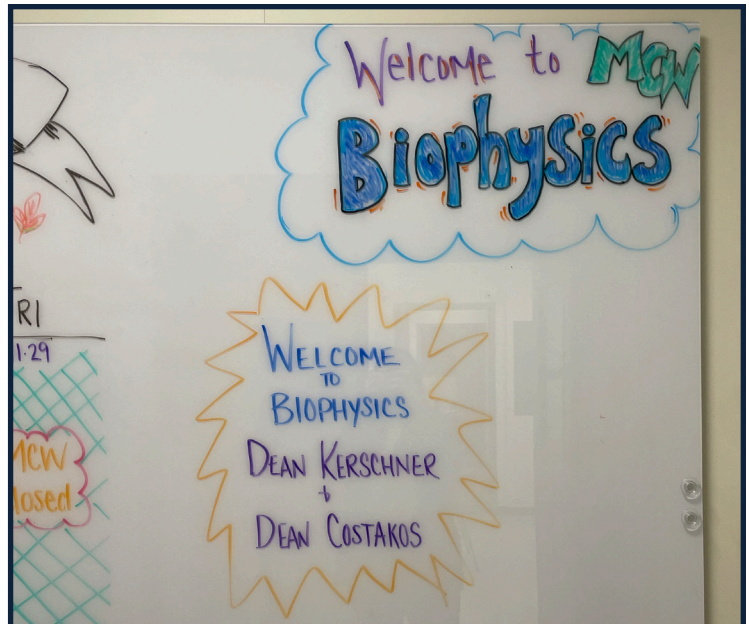
- Mona Al-Gizawiy, PhD, Assistant Professor
- Nikolai J. Mickevicius, PhD, Assistant Professor
- Kathleen M. Schmainda, PhD, Professor
- Jason W. Sidabras, PhD, Assistant Professor



Dr. Al-Gizawiy discussed the work of Dr. Schmainda and the entire team's efforts in treating glioblastoma. Dr. Schmainda and colleagues showed that the novel iron mimetic gallium maltolate (GaM) has potent effects as a tumor suppressor in treatment-resistant glioblastoma, an aggressive brain tumor with dismal prognosis. The work serves as the springboard for a Phase I clinical trial launched in 2022 at MCW to evaluate the potential of GaM in combination therapy. This is the first investigator-initiated clinical trial using GaM where all the preclinical to clinical work was done at MCW. Dr. Al-Gizawiy shared that their team and work in biophysics is the epitome of academic medicine. Dr. Sidabras discussed the GaM work benefits from the state-of-the-art magnetic resonance coil technology being developed in his lab. This new coil has superior sensitivity to allow the team to monitor tumor growth and treatment response. This patented technology has been developed for use in animals at the 9.4T level and is being translated for human use.

Dr. Mickevicius shared that his research efforts include optimizing MRI for quantitative results and reducing the time needed to perform experiments. He has included a calibration step to make the scanner more accurate through the use of an MRI safe temperature controller.

This group's research is of particular importance as it relates to pediatric practice as it has increased quality of life benefit. This work is a fantastic model of our bench-to-bedside care.



Next, we visited with the structural biology team, which includes:

- Jimmy B. Feix, PhD, Professor
- Candice S. Klug, PhD, James S. Hyde Professor of Biophysics; Director, National Biomedical EPR Center; Program Director, Biophysics Graduate Program; Vice Chair for Research in the Department of Biophysics
- Vanessa A. Leone, PhD, Assistant Professor
- Michael T. Lerch, PhD, Associate Professor
- Francesca M. Marassi, PhD, Professor, Chair, and Eminent Scholar; Associate Director, MCW Cancer Center Shared Resources
- Fabrizio Marinelli, PhD, Assistant Professor
- Kyungsoo Shin, PhD, Assistant Professor
- Jason W. Sidabras, PhD, Assistant Professor
- Gopinath Tata, PhD, Assistant Professor

Dr. Lerch and colleagues have used EPR and other biophysical methods to develop a new biased agonist for the β_2 -adrenergic receptor, a G protein coupled receptor that is expressed in cardiac myocytes and plays essential roles in the regulation of cardiac function by the sympathetic nervous system. The study deepens our understanding of G protein specificity and bias, and it accelerates the design of therapeutic drug precursor ligands that select preferred signaling pathways.

I celebrated the hard work of Dr. Candice Klug who has continued to build the Electron Paramagnetic Resonance (EPR) Center after years of development. Dr. Marassi has brought solid-state NMR to the Department, thus adding to the arsenal of technologies for structural characterization. MCW is a leader in functional MRI, EPR, and NMR.

The efforts of this group are a wonderful example of marrying computation with experimentation by using computational modeling.



We then met with the redox biology and drug development group, which includes:

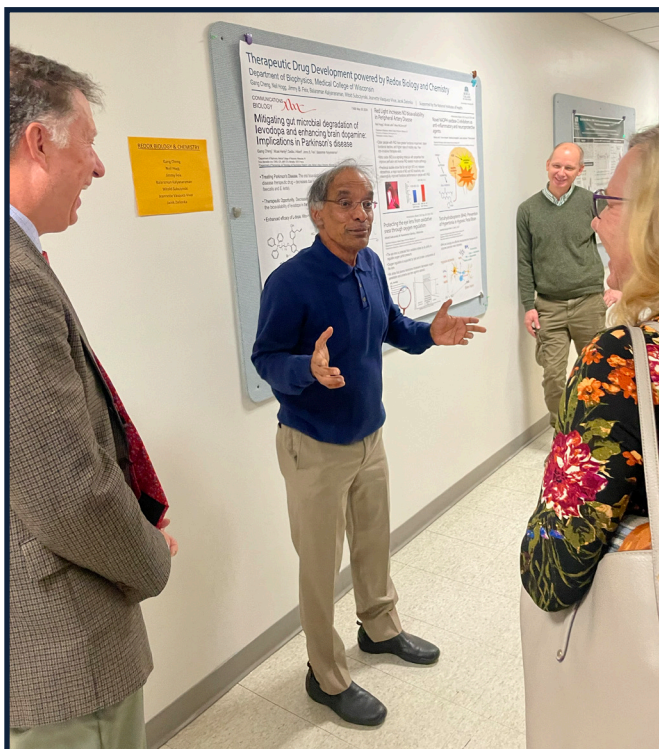
- Gang Cheng, PhD, Assistant Professor
- Neil Hogg, PhD, Professor; Director, Redox Biology Program; Associate Dean of Academic Affairs, School of Graduate Studies; Vice Chair for Education in the Department of Biophysics
- Jimmy B. Feix, PhD, Professor
- Balaraman Kalyanaraman, PhD, Harry R & Angeline E. Quadracci Professor in Parkinson's Research
- W. Karol Subczynski, PhD, DSc, Professor
- Jeannette Vasquez-Vivar, PhD, Professor; Associate Director, Redox Biology Program; Vice Chair for Faculty Affairs in the Department of Biophysics
- Jacek Zielonka, PhD, DSc, Assistant Professor; Director, Redox & Bioenergetics Shared Resource

Alongside colleagues, Dr. Kalyanaraman has developed a new mitochondria-targeted small molecule (mito-honokiol, also called mito-HNK) that reversibly inhibits levodopa degradation by the gut bacteria, *Enterococcus faecalis*. Combined administration of mito-HNK and levodopa in mice decreases metabolism of levodopa to dopamine in the gut and enhances both the uptake of levodopa and its conversion to dopamine in the brain. This study, published in *Communications Biology*, suggests a potential therapeutic pathway for enhancing the efficacy of Parkinson's disease therapy. The team's aspirations include drug development for the management of Parkinson's disease. The lab's efforts are all housed within the Biophysics Department thanks to their chemistry lab with two dedicated chemistry hoods. Our time concluded with a visit to some of the labs and an opportunity to view the various pieces of equipment.

In addition to the leadership of Dr. Marassi, I am grateful for the entire team who made this visit happen, particularly the dedicated staff members, Shannon Gustavson, Administrative Associate; Laura Borst, Business Operations Coordinator; Heidi Geiger, Department Administrator; and Lydia Washechek, Grants Operations Coordinator. I deeply appreciate the efforts it took to plan this morning.



The Department of Biophysics embodies the best of MCW. I am proud of their energy of innovation and spirit of collaboration as they work to advance MCW's mission of knowledge changing life.



By The Numbers: Biophysics

- 19** Primary Faculty Members
- 13** Secondary Faculty Members
- 1** Emeritus Faculty
- 5** Adjunct Faculty
- 7** Postdoctoral Researchers
- 12** Lab Staff
- 17** Graduate Students
- 114** Graduate Student Alumni