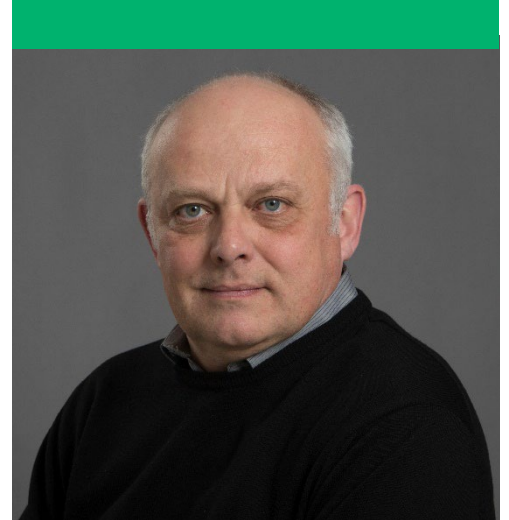


Lothar A. Blatter, MD, Dr. med.

The John H. and Margaret V. Krehbiel
Professor of Cardiology



Advancement of Medicine

In 2023, our research group continued work in basic and translational research in the field of cardiac physiology and pathophysiology. We focus on the mechanisms that regulate calcium in the cells of the heart, and the mechanisms that regulate the contraction and the pump function of the heart. We also focus on the dysregulation of calcium that result in irregular heartbeat, or cardiac arrhythmia, especially atrial fibrillation, which is the most common form of arrhythmia in humans. A central theme in this context is the study of the pathological condition of cardiac alternans. Pulsus alternans is a condition wherein the heartbeat cyclically varies between weak and strong and often precedes full development of arrhythmias.

In 2023-24 we published five original papers in peer-reviewed journals that provide novel insights into the mechanisms of cardiac alternans. Furthermore, we made several presentations at scientific conferences.

Research

The investigation of basic and translational aspects of the mechanisms of disturbed calcium signaling in cells of the heart that lead to irregular heartbeat will continue to be at the center of our research activities. Cardiac arrhythmia is a serious clinical problem that affects a significant portion of our population, and its prevalence is on the rise given the overall aging population. This applies especially to atrial fibrillation, the most common form of cardiac arrhythmia. Our research will make important new contributions to the mechanistic understanding of atrial fibrillation mechanisms at the cellular and at the organ level.

Grants

Our research is currently supported by two active National Institutes of Health R01 grants:

- “IP3 receptor, NOX2 and calcium signaling domains in atrial physiology and pathophysiology.”
- “Atrial excitation-contraction coupling, calcium signaling and electro-mechanical alternans.”

I am co-principal investigator on both grants, along with Kathrin Banach, PhD, associate professor in the department of Internal Medicine Cardiology Division. These two funded NIH grants reflect successful collaborations between Rush faculty in basic science and clinical departments and provide a total amount of funding of \$ 5,411,327 for four years.

Publication Highlights — Abbreviated

“The 'reverse FDUF' mechanism of atrial excitation-contraction coupling sustains calcium alternans - a hypothesis,” *Biomolecules* 13(1), 7 (2023).

“Activation of small conductance Ca^{2+} -activated K^{+} channels suppresses Ca^{2+} transient alternans in ventricular myocytes,” *The Journal of Physiology* 601(1): 51-67. Editor's choice article and featured in *J. Physiology's* 'Physiology Shorts' video clip. (2023).

“Calcium- and voltage-driven atrial alternans: insight from $[\text{Ca}]_i$ and V_m asynchrony. *Physiological Reports* 11, e15703 (2023).

“Increased risk for atrial alternans in heart failure: the role of Ca^{2+} /calmodulin-dependent kinase II and inositol-1,4,5-trisphosphate signaling,” *Biomolecules* 14, 53 (2023).

“Role of mitochondrial ROS for calcium alternans in atrial myocytes,” *Biomolecules* 14, 144 (2024).

Speaking Engagements and Presentations

- “Enhanced CaMKII Activity and IP3 Signaling in Heart Failure Increase Risk of Atrial Alternans,” International Society for Heart Research-North American Section (ISHR-NAS) 2023.
- “Mitochondrial ROS and Calcium Alternans in Atrial Myocytes. International Society for Heart Research-North American Section (ISHR-NAS) 2023.
- “Enhanced CaMKII activity and IP3 signaling in heart failure increase risk of atrial alternans,” Chicago Regional Cardiovascular Research Symposium 2023.



- “Mitochondrial ROS and Calcium Alternans in Atrial Myocytes,” Chicago Regional Cardiovascular Research Symposium 2023.

The Year Ahead: 2024 and Beyond

With your support I will continue to strive to maintain a strong, productive, extramurally funded research program and to continue to provide an excellent training environment for my research group.

With Gratitude

I would like to take this opportunity to express my gratitude to your family for generously supporting my research activities in the field of cardiac physiology and cardiac disease.