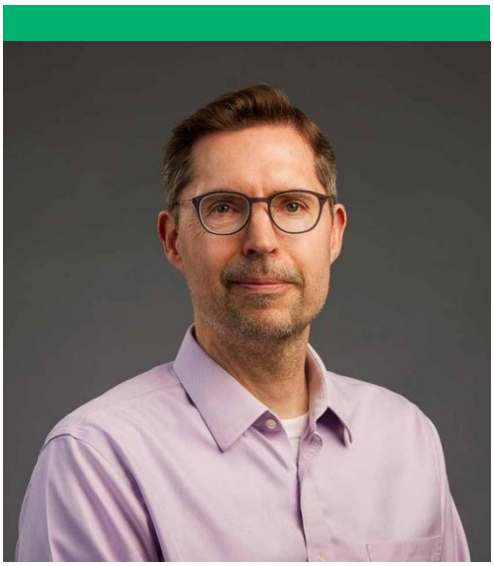
RUSH

Dirk Gillespie, PhD

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



Advancement of Medicine

As I near the end of my first year in the professorship your family has endowed, I am excited for the opportunity to share updates on my work.

First and foremost, I want to thank you for your incredibly generous support of Rush and cardiac research. Unfortunately, heart disease continues to be the leading cause of death for Americans and Chicagoans, and your support of cardiac research is vital for the development of future therapies. Over the 30 years of this endowed professorship, researchers and clinicians at Rush and elsewhere have made tremendous strides toward new therapies, and I have spent the last 22 years at Rush working toward that goal.

My work has always centered on trying to see what experiments cannot see by performing computer simulations, replicating what happens in experiments using equations. At first, computers may seem like an unlikely tool for cardiac research. But over the last 30 years, computers have become so powerful that they can now see what happens at molecular scales that experiments cannot resolve, helping us understand the underlying processes.

For example, **Lothar Blatter, MD, Dr. med.**, the previous holder of the Krehbiel Professorship, used a microscope to examine cardiac cells and track their molecular signals. However, the laws of physics prevented us from seeing what occurs at resolutions below a certain point; the pictures became blurry as we zoomed in. I am now simulating the exact same processes he looked at, but the resolution of a computer simulation is hundreds of times sharper than the experiments. With such fine details, I can deduce exactly *why* things happened at the molecular level.

Today, computer simulations and experiments complement each other across virtually all scientific fields. And that insightful coordination has continued in my work over the last year — **work that was only made possible by this endowment** — as exemplified by two projects.

RUSH

Research Projects

The first project is a new collaboration with **Bjorn Knollmann, MD, PhD**, at Vanderbilt University, who works on experimental therapeutics for cardiac arrhythmias. The Krehbiel endowment enabled me to attend a scientific meeting I would not have otherwise been able to attend. There, Dr. Knollmann described how he and his group had developed a new class of anti-arrhythmic drug candidates, but even with all their experimental resources, they had not been able to understand how these compounds got to their target deep inside a large protein. Dr. Knollmann asked me whether my computer simulations could help, as this lack of knowledge was preventing publication of the work. Within a few weeks of returning home, I demonstrated the answer his group had sought for several years, as well as why they had not been able to measure it in experiments.

The second new collaboration began at the same conference. I presented new data where my simulations made novel predictions about an important process in heart cells. Coincidentally, **Peter Szentesi, PhD**, from the University of Debrecen in Hungary, presented experimental data that seemed to show the same phenomenon, albeit not in cardiac cells. The endowment later funded a trip to Hungary to discuss the details of Dr. Szentesi's data. Since then, I have acquired additional similar rare, high-scan-rate experiments from heart cells, analyzed them alongside Dr. Szentesi's data and confirmed my predictions. I am now writing a manuscript for publication in a peer-reviewed journal.

Overall, my first year with the endowment has changed the course of my research significantly because it brought new collaborations with researchers in experimental therapeutics and researchers sharing their rare, high-quality experimental data. Both have been long-standing goals for me, and thanks to the endowment, these are now possible.

RUSH

The Year Ahead: 2026 and Beyond

It is vital that this work be complementary: experiments and computer simulations must strengthen each other. My simulations are based on experimental data to provide an accurate representation of reality and, in turn, offer insights into cellular processes that can be tested in follow-up experiments. The new experimental collaborations will make it possible to close this virtuous circle.

Over the next year, I will continue working with Dr. Knollmann on drug candidates. Moreover, I will delve deeper into the consequences of the mechanism predicted by the simulations, as it appears to be a novel target for new drugs.

With Gratitude

I want to close by reiterating my sincere gratitude for your generous support of Rush, cardiac research and your parents' legacy. Your support is truly advancing my work. Thank you.