

KEITH REIMER, M.D.

1946-2002

Keith Arnold Reimer, M.D., Ph.D., Professor of Pathology at Duke University Medical School, internationally recognized cardiovascular scientist, pathologist, and teacher, died on March 15, 2002 of metastatic renal cell carcinoma at the age of 56. Keith began his career in experimental pathology studying ischemic injury of the kidney, however he quickly shifted his focus to myocardial ischemic injury, the field in which he went on to make his major scientific contributions. After completing the MD/PhD program at Northwestern University in Chicago, Keith joined the faculty at Duke University in 1975 as Assistant Professor of Pathology. Early in his career, working in collaboration with Dr. Robert B. Jennings, he published landmark studies describing and characterizing the "wavefront phenomenon" of myocardial ischemic cell death. These studies, published in two papers (*Circulation* 56: 786-794, 1977; and *Laboratory Investigation* 40: 633-644, 1979), have been cited more than 1000 times. During the early 1980s, Keith developed methods to measure baseline predictors of infarct size, such as area at risk and collateral flow, that have become the standard for generating reliable and reproducible data to test cardioprotective interventions. The effort to discover cardioprotective interventions led to one of Keith's most notable achievements – the description of one of the strongest and most reproducible interventions for reducing infarct size: ischemic preconditioning. Numerous investigators and laboratories have worked to better understand this remarkably effective intervention, and the ever-expanding number of studies on ischemic preconditioning, in a wide variety of tissues, have consistently confirmed the original observation that brief periods of ischemia and reperfusion are not detrimental, but are actually markedly protective. The original article describing the phenomenon of ischemic preconditioning, "Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium" (*Circulation* 74: 1124-1136, 1986) has been cited more than 3700 times (the most cited paper in *Circulation*).

Keith was an active member of the ISHR since 1976, and was elected a Councilor of the American Section in 1979, serving until 1985. He was a finalist for the Richard Bing Young Investigator Award of the ISHR in 1980. Keith served as Secretary of the American Section from 1985-1994, and as a member of the Council of the International Society from 1989-1995. In 1997, he became President-Elect of the American Section and was the sitting President of the American Section, as well as a member of the International ISHR Council, when he died.

About the Award...

Each year, the International Council selects a speaker to deliver the Keith Reimer Distinguished Lecture at the World Congress or at the annual section meeting of one of the three largest ISHR Sections. The purpose of this lecture is to honor the memory of Dr. Reimer and to recognize his contributions to cardiovascular research. The topic of the lecture must be in the field of ischemia, coronary hemodynamics, cardiac metabolism, or contractile mechanisms. The speaker receives a plaque and \$1,000 honorarium in addition to travel expenses.

*This award is funded by a generous contribution from
Chugai-Pharmaceutical Co.*



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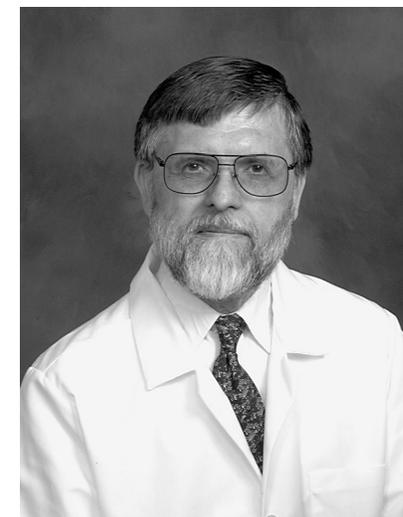
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THE KEITH REIMER DISTINGUISHED LECTURE 2016



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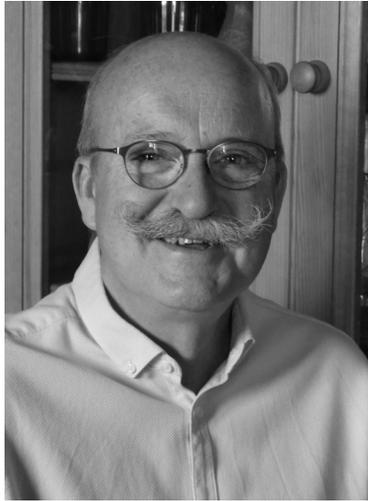


Honored Speaker

Dr. Rodolphe Fischmeister

**“Cyclic nucleotide micro-
domains & phosphodiesterases:
Small sinks with smart drains
can do a lot!”**

RODOLPHE FISCHMEISTER, PH.D. BUENOS AIRES, ARGENTINA



Rodolphe Fischmeister says he “never learned biology!” He studied math and physics instead, and graduated as an electrical engineer (1978). He received his PhD in 1980 at the University of Paris-Sud in Orsay, France, for mathematical modelling of cardiac electrical activity with Guy Vassort, and then performed a first postdoc with Magda Horačková

at Dalhousie in Halifax, Canada (1981-1982), where he developed a theoretical model of the L-type Ca^{2+} current ($I_{\text{Ca,L}}$) and intracellular calcium diffusion in heart cells. His desire to move to the experimental field was fulfilled when Robert L. DeHaan offered him a postdoc position in his lab at Emory, Atlanta (1982-1983). There, together with the group of Louis J. DeFelice, he developed an original double patch-clamp method to simultaneously measure single channel currents at the surface membrane and intracellular spontaneous action potentials in chick embryonic heart cells. With William Clusin, he explored the effect of caffeine on ion currents and provided the first evidence of a current in cardiac cells due to the activity of the $\text{Na}^+/\text{Ca}^{2+}$ -exchanger.

In 1983, Dr Fischmeister returned to France and joined the lab of Guy Vassort at the University of Paris-Sud in Orsay after obtaining a permanent position as research associate at INSERM. He has been faithful to INSERM ever since and has climbed up the steps of the ladder to become Director of Research '2nd class' in 1989, '1st class' in 1997 and 'exceptional class' in 2011. He left the lab of Guy Vassort in 1992 to build his own lab at the Faculty of Pharmacy of the University Paris-Sud, which is located in Châtenay-Malabry. His lab, which started with 10 people in 1992 and now includes more than 50 people, has been continuously funded by INSERM since then. In addition, his lab has regularly raised additional funds from

several foundations and funding agencies (including ANR, AFM, FRM, Fondation Leducq and others) as well as from the pharmaceutical industry. In 2015, he stepped down to allow Ana Maria Gomez to head the lab, and he is now acting as deputy director. Meanwhile, in 2010, Dr Fischmeister founded an interdisciplinary laboratory called “The Laboratory of Excellence in Research on Medication and Innovative Therapeutics” (LERMIT), which involves 16 different labs with high-profile biologists, chemists and physico-chemists joining forces to collectively explore new therapeutic avenues. The LERMIT received a €19Mn budget from the “*Investments in the Future programme*” of the French Government for the period 2011-2019. Some of these funds are used for the development of new molecules in heart failure.

The main focus of Dr Fischmeister's research is the neurohumoral regulation of cardiac function and the adaptation and remodelling processes taking place under pathophysiological conditions, such as during hypertrophy and heart failure. Using cellular models (frog, rat, mouse, and Human cardiomyocytes), his group developed original approaches to dissect the mechanisms involved in the sympathetic and parasympathetic regulation of $I_{\text{Ca,L}}$. Combining patch-clamp with intracellular perfusion of a single myocyte via the patch-clamp pipette, in 1986 they discovered the cGMP/cAMP antagonism on $I_{\text{Ca,L}}$. Using a millisecond external perfusion system, they were able to determine the sequence of events in the β -adrenergic cascade leading to the positive inotropic response. In 1996, double barrelled microperfusion of a single cardiomyocyte led to the first demonstration in a living cell of an intracellular compartmentation of cAMP. Combining patch-clamp with FRET-based fluorescence imaging led to the first real time measurements of intracellular cAMP in an intact cardiomyocyte. Expression of cyclic nucleotide gated channels from olfactory neurons in cardiomyocytes allowed, for the first time, real time monitoring of cAMP and cGMP at the sarcolemmal membrane. Step by step, Dr Fischmeister's group has established unique expertise in cellular cardiac physiology and their work has received great international recognition.

Dr Fischmeister has published over 140 papers in peer-reviewed international journals (160 in total), accumulated >7000 citations (with 20 papers cited >100 times), and his current H-index is 50. He has been invited to 150 scientific meetings and

presented >100 seminars around the world. He has served as external referee for NIH, NSF, MRC, Wellcome Trust, CNR, Telethon, and the Government of Canada, among others. He has reviewed papers for >20 different journals and is currently Associate Editor in *Cardiovascular Research*. He has been President of an INSERM Study Section (2008-2012). He is an elected member of a number of professional organisations, member of the Academia Europaea, and President-Elect of the European Section of the ISHR. He has received several prizes and awards (Jeanne-Philippe Beziat Cardiology Prize 2012, Alain Castaigne Prize 2014). He has also trained 30 young post-graduate researchers, half of them coming from foreign countries.

Rodolphe Fischmeister has been a leader in the field of cardiac cellular physiology since its inception. He has studied Ca^{2+} channels and signalling in the heart and the pathways that stimulate production of the second messengers cGMP, cAMP, and NO. He showed how these pathways impact normal heart contraction and the diseased heart. He performed the initial studies that carried the concept of compartmentalized cAMP signalling from an obscure hypothesis to demonstrated fact. He discovered the determinant role of cyclic nucleotide phosphodiesterases in this process and showed that a loss of compartmentation occurs during pathological cardiac hypertrophy. He is currently exploring strategies to restore cAMP compartmentation by activation of specific phosphodiesterases as a novel therapeutic approach in heart failure. Dr Fischmeister's background in engineering has given him the edge needed to bypass traditional thinking in physiology and create new methodologies that have pushed the field forward.

Previous Award Winners...

- Gerald Dorn, MD: 2015**
- Fabio Di Lisa, MD: 2014**
- Karin Sipido, MD, PhD: 2013**
- Metin Avkiran, DSc, PhD: 2012**
- Charles Murry, MD, PhD: 2011**
- Richard Moss, PhD: 2010**
- Elizabeth Murphy, PhD: 2009**
- David Eisner, PhD: 2008**
- Eduardo Marbán, MD: 2007**
- Garrett Gross, PhD: 2006**
- Masao Endoh, MD, PhD: 2005**
- R. John Solaro, PhD: 2004**
- Gerd Heusch, MD, PhD: 2003**
- Roberto Bolli, MD: 2002**