

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 six ISHR Sections on a rotating basis. 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
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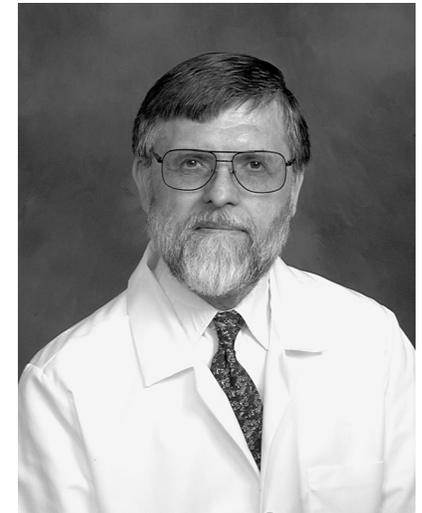
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ISHR

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THE KEITH REIMER DISTINGUISHED LECTURE 2019



Keith Reimer, M.D. 1946-2002



Honored Speaker

Dr. Christoph Maack

“Mitochondrial redox regulation
in heart failure”

CHRISTOPH MAACK, M.D.

2019 HONORED SPEAKER
BEIJING, CHINA



Christoph Maack received his MD at the **University of Cologne** (Germany) in 2000. From 2000 to 2017, he mainly worked at the **Department of Cardiology at the University of the Saarland in Homburg**, Germany (Director: Professor Michael Böhm), first as an Assistant- (2000-2002; 2005-2012) and from 2012 on as a Senior Physician. From

2002 to 2005, he performed a post-doctoral research fellowship in the Department of Cardiology at **Johns Hopkins University in Baltimore, MD, USA**, in the laboratory of Brian O'Rourke, PhD. From 2006 on, he established his own working group in Homburg with the support of the **Emmy Noether Programme** of the German Research Foundation (DFG). From 2012 on, he held a **DFG Heisenberg Professorship** on Cardiovascular Physiology and Bioenergetics in Homburg, Germany. Since 2017, Dr. Maack is the Chair of Translational Science and the Spokesperson of the **Comprehensive Heart Failure Center (CHFC)** at the **University Clinic in Würzburg, Germany**.

Christoph Maack's work focuses on **cellular defects in chronic heart failure**, with a special emphasis on the mechanisms of **contractile, mitochondrial and metabolic dysfunction in heart failure**. In his early research (1997-2003), his focus was on the pharmacology of β -adrenergic receptors, characterizing differential receptor interaction properties, (inverse) agonist activities and antioxidative efficacies of clinically used **β -blockers in human ventricular myocardium *in vitro***, but also in healthy volunteers and patients with heart failure *in vivo*. In the early 2000s, his focus shifted towards different **mechanisms and sources of reactive oxygen species (ROS) formation and elimination in the failing heart**, such as by NADPH oxidase and mitochondria. During his post-doctoral

years in the lab of Brian O'Rourke at Johns Hopkins University, Baltimore, US (2002-2005) he gained expertise in the mechanisms of excitation-contraction (EC) coupling and how **cytosolic Ca^{2+} and Na^{+} handling regulate mitochondrial function**. Through this work and the studies performed after his return to Germany, he established the concept that the **defects of EC coupling that occur in heart failure hamper mitochondrial Ca^{2+} uptake** and thereby, energy supply and demand matching, potentially contributing to the energetic deficit which is characteristic for heart failure. Furthermore, together with the group of Brian O'Rourke he discovered that since Ca^{2+} -dependent Krebs cycle stimulation also regenerates NADPH for the antioxidative capacity, defective mitochondrial Ca^{2+} uptake also accounts for **increased mitochondrial ROS emission**, which has an important impact on arrhythmias, contractile dysfunction and cardiac remodeling during the development of heart failure. In more recent work, he and his group discovered a key mechanism how an **increase in cardiac afterload increases mitochondrial ROS emission**, a mechanism that is linked to the reversal of the mitochondrial transhydrogenase (an enzyme linking the NADH and NADPH pools, respectively). In his ongoing research in collaboration with Lucie Carrier, Thomas Eschenhagen (Hamburg, Germany) and Björn Knollmann (Vanderbilt University, Nashville, US), Dr. Maack has discovered a mechanism how in hypertrophic cardiomyopathy, sarcomeric mutations can induce ventricular arrhythmias through mitochondrial oxidation. An important goal of his research is to identify potential sites of intervention that could ameliorate the progression of heart failure and arrhythmias, such as targeting cytosolic or mitochondrial ion handling, or drugs targeted to mitochondria that reduce ROS formation and/or emission.

For his research, Professor Maack was awarded the Franz-Maximilian-Groedel- (2007), Albert-Fraenkel- (2014) and the Arthur-Weber Awards (2015) of the **German Cardiac Society**, respectively. He has been the chair of the Working Group of Myocardial Function and Energetics of the German Cardiac Society (2011-2013) and was a Board member of the

Heart Failure Association (HFA) of the **European Society of Cardiology (ESC)** from 2010-2016. From 2011-2014 he was the Coordinator of the Translational Research Committee of the HFA, and from 2014-2016 served on the **Executive Committee of the HFA Board** as the **Chair of the Basic Science section**. In the years between 2013-2016, Dr. Maack was the main organizer of the **Heart Failure Winter Meeting** of the HFA in Les Diablerets, Switzerland. Since 2015 he is a **Fellow of the HFA** of the ESC and serves on the Programme Committee of the German Cardiac Society. In 2018, he was elected a member on the Council of the **International Society of Heart Research (ISHR)**, European Section (ES). Furthermore, Dr. Maack was vice chair of the **Gordon Research Conference** on Cardiac Regulatory Mechanisms in New London, NH, USA and will be chair of the upcoming (same) GRC in 2020.

Previous Award Winners...

Steven Houser, PhD: 2018

Brian O'Rourke, PhD: 2017

Rodolphe Fischmeister, PhD: 2016

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