

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 1700 times.

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 speaker's section meeting. 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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THE KEITH REIMER DISTINGUISHED LECTURE 2006



Honored Speaker

Dr. Garrett Gross

“Acute and Chronic Opioid-
Induced Cardioprotection”

GARRETT GROSS, PH.D.

2006 HONORED SPEAKER
TORONTO, ONTARIO



Dr. Gross graduated with his Ph.D. in Pharmacology from the University of Utah in 1971. He subsequently performed two postdoctoral fellowships, one at the Warner-Lambert Research

Institute under the direction of Dr. Martin Winbury, and the second at the University of Washington with Dr. Eric O. Feigl. Both of these imminent scholars stimulated Dr. Gross's interest in the control of coronary blood flow and in pharmacological mechanisms for reducing injury to the ischemic myocardium. Dr. Gross joined the faculty in Pharmacology and Toxicology at the Medical College of Wisconsin in 1973 and rose to the rank of Professor in 1980. He has been an active and continuously NIH-funded investigator at the Medical College of Wisconsin for the past 33 years.

Dr. Gross's major area of research concerns mechanisms by which endogenous substances released by the heart can either injure or protect the heart during ischemia and/or reperfusion, and he has been a leader in understanding mechanisms by which the heart adapts itself to an ischemic insult, a phenomenon termed ischemic preconditioning (IPC). In this regard, Dr. Gross's laboratory was the first to demonstrate that an ATP-sensitive potassium channel (K_{ATP} channel) was a critical trigger and effector of IPC. This breakthrough has been repeated by a number of investigators and has stood the test of time as one of the key components of this remarkable cardioprotective phenomenon. This continues to be an active area of investigation in his laboratory and it is hoped that a pharmacological activator of this channel will be developed that is safe and efficacious and will be able to mimic the potent cardioprotective properties of IPC. In support of this concept, a potent opener of this channel, nicorandil, has been on the market in Japan and Europe for the treatment of stable angina since the

1990s and Dr. Gross's laboratory did much of the pioneering work on the development of this compound in the early 1980's. More recently, this was the first drug (IONA Trial) to demonstrate a long-lasting cardioprotective effect in patients with angina in a well-controlled clinical trial.

Dr. Gross's was also the first laboratory to identify a role for endogenous opioids in mediating the cardioprotective effects of IPC in several animal models. His laboratory showed that exogenous opioids such as morphine also possessed potent cardioprotective properties and that these effects were mediated via the action of opioids on both sarcolemmal and mitochondrial K_{ATP} channels. These findings led investigators in many other laboratories to study the role and mechanisms responsible for these potent cardioprotective properties of opioids, and suggest that it may be possible to use novel opioid compounds which lack CNS effects as cardioprotective agents in the future. Dr. Gross's laboratory also was the first to demonstrate that the cardioprotective effect of chronic morphine treatment persisted for 120 hours which suggests that this type of drug might be used prophylactically prior to cardiac surgery to put the heart in a protected state a day or two prior to and even after open heart surgery.

In his most recent work, for which he was awarded the prestigious NIH MERIT Award, Dr. Gross has uncovered a new endogenous cardioprotective pathway which appears to be mediated by CYP 450 isoforms in the heart. His data show that a product produced by CYP w-hydroxylases, 20-HETE, produces myocardial injury and that blocking the synthesis of, or the receptor for, this compound produces a marked reduction in infarct size in dog hearts. These data may lead to a new therapeutic target for drug development.

Over the past 33 years Dr. Gross's work has resulted in approximately 360 full-length peer reviewed journal articles and reviews and 27 book chapters. Dr. Gross has been an invited speaker at more than 70 universities and phar-

maceutical and biotechnology companies. He has been a consultant at over 20 pharmaceutical companies and has mentored 15 Ph.D. students and 10 postdoctoral fellows, all of whom were funded by fellowships from the American Heart Association and the Pharmaceutical Manufacturers Association Foundation of America. Dr. Gross is a very active reviewer for all the major cardiovascular journals including *Circulation Research*, *Cardiovascular Research* and *JMCC*, and he currently serves on the Editorial Board of 8 journals and has been an Associate Editor of the *American Journal of Physiology (Heart and Circulatory)* for the past 7 years. Dr. Gross is a Fellow of the American Heart Association, a Founding Fellow of the International Society of Heart Research and is a member of the American Society of Pharmacology and Experimental Therapeutics and the American Physiological Society. He served as member of the NIH Pharmacology Study Section for 4 years and continues to be an active *ad hoc* reviewer for the NIH on PPGs and RO1s related to the myocardial ischemia field.

Previous Award Winners...

Masao Endoh, MD, PhD

(Osaka, Japan: 2005)

R. John Solaro, PhD

(Brisbane, Australia: 2004)

Gerd Heusch, MD, PhD

(Strasbourg, France: 2003)

Roberto Bolli, MD

(Madison, WI: 2002)