

## ISHR Outstanding Investigator Award

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The purpose of this award is to recognize an outstanding scientist who (i) is making major and independent contributions to the advancement of cardiovascular science, and (ii) is leading a growing research program likely to play a major role in the future. The main criteria for selecting awardees are scientific excellence, independence, and potential for future research contributions. While the Peter Harris Award recognizes lifelong accomplishments and the Richard Bing Award recognizes young investigators, the Outstanding Investigator Award (presented annually) is targeted at established investigators who are in the intermediate phase of their academic career.

In non-Congress years, the Outstanding Investigator Award is presented at the meeting of the ISHR Section to which the winner belongs. The winner presents a major lecture and receives a \$5,000 honorarium and a plaque. An announcement of this Award is published in *Heart News and Views*, and posted in the ISHR website. The winner receives free registration and reimbursement for travel expenses (up to a maximum of \$1500 when the recipient delivers the lecture at his/her local Section meeting, and \$3,000 when inter-continental travel is required).

Nominations for the Outstanding Investigator Award are sought by the Secretary General from members of the International Council, members of the Editorial Board of the *Journal of Molecular and Cellular Cardiology*, and the Councils of ISHR Sections. In addition, the Secretary General publishes an open invitation in the ISHR Website for members to submit nominations.



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ISHR

International Society for Heart Research

## The Outstanding Investigator Award 2011



Award Winner

**Dr. Walter J. Koch**

“Is it Translation or Perseverance?  
GRK2 and S100A1 as Targets for Heart  
Failure Gene Therapy”

## Walter J. Koch, Ph.D.

## 2011 Award Winner Philadelphia, PA

Dr. Walter J. Koch is the W. W. Smith Professor of Medicine and currently serves as Director of the Center for Translational Medicine and Vice Chair for Research in Department of Medicine at Thomas Jefferson University. Dr. Koch received his Ph.D. in Pharmacology and Cell Biophysics in 1990 in the Lab of Dr. Arnold Schwartz at the University of Cincinnati. Following this he began a Howard Hughes Post-Doctoral Fellowship in the Laboratory of Dr. Robert J. Lefkowitz at Duke University Medical Center. In 1995 he was recruited to start a molecular cardiovascular biology laboratory in the Department of Surgery at Duke. While a faculty member at Duke, Dr. Koch rose quickly and became a tenured Full Professor of Surgery within 6 years of starting his independent laboratory. Dr. Koch moved to Jefferson in 2003 to build the Center for Translational Medicine where he has recruited 12 primary tenure-track faculty. These Center faculty members under Dr. Koch's leadership carry out basic and translational studies in cardiovascular disease.

Dr. Koch has received numerous honors and awards prior to being named the 2011 Outstanding Investigator of the International Society of Heart Research including presenting the Thomas Smith Memorial Lecture at the 2009 American Heart Association Meetings. Dr. Koch was presented with the Davison Award for Teaching while at Duke and won the Jefferson Medical College Inaugural Career Achievement Award in Biomedical Sciences in 2010. He has also been named a Fellow of the AHA and last year was named a Fellow of the ISHR. Dr. Koch is currently well funded through the NIH and holds a MERIT Award from the NHLBI and is the Principal Investigator of a Program Project Grant. He also is a named inventor of 8 patents.

In 2010, Dr. Koch ended his tenure as Chair of the CCHF NIH study section and reviews grants for several international committees. He currently is a member of the Recombinant DNA Advisory Committee (RAC) of the NIH. He is an Associate Editor of Circulation Research and an Executive Editor of Clinical and Translational Science. He is also currently the Co-Chair of the Basic Cardiovascular Science (BCVS) Council of the American Heart Association.

Specifically in the Koch Laboratory, studies are focused on the adrenergic receptor system in heart failure. Over the last two

decades the Koch lab has focused on the role of G protein-coupled receptor (GPCR) kinases (GRKs) and the role they play in normal and failing heart function including how they regulate adrenergic receptors. They have found that one GRK, GRK2, is pathological in the heart both acutely and chronically after myocardial stress/injury. More recently, they have uncovered novel roles for GRKs in the heart independent from their receptor kinase functions. Overall, Dr. Koch has published over 250 peer-reviewed articles that has led to over 12,000 citations. This includes 36 articles cited over 100 times and he currently as an h index of 57 (57 papers references at least 57 times).

While a post-doctoral fellow, Dr. Koch showed in a paper published in Science in 1995 that manipulation of GRK2 activity in the heart could have profound effects on *in vivo* cardiac function. Dr. Koch developed and discovered a peptide inhibitor of GRK2, named the  $\beta$ ARKct, which has led to the elucidation of several important aspects of GRK2 in the heart including it being pathological following cardiac injury. Subsequently, working collaboratively with Dr. Howard Rockman, Dr. Koch went on to show that inhibition of GRK2 in the heart could rescue several mouse models of heart failure. Dr. Koch's work also heavily involved cardiac gene therapy research where his team at Duke developed novel models of coronary artery delivery of viruses carrying potentially therapeutic transgenes. In 2009, Dr. Koch published a landmark paper showing that chronic inhibition of cardiac GRK2 using  $\beta$ ARKct delivered via an adeno-associated viral (AAV) vector could rescue a heart failure model in the rat.

Dr. Koch has also studied the role of GRK2 in other organs during heart failure progression and in a study published in 2007 in Nature Medicine, his lab defined a pathological role for this kinase in sympathetic nervous system regulation and catecholamine release from the adrenal gland. Most recently, Dr. Koch's team, in a paper recently published in Circulation Research, has shown that GRK2 in the heart is not only important in chronic heart failure but its activity is pathological in the acute setting as it acts as a pro-death kinase in myocytes after ischemic injury.

In addition to landmark studies detailing the importance of GRK2 in the cardiovascular system, Dr. Koch has also shown a

second GRK, GRK5, to be critical. This includes demonstrating that this kinase has the unique property to localize to the nucleus of myocytes where it exerts a novel, non-GPCR function as a Class II HDAC kinase to promote maladaptive cardiac hypertrophy. This was published in 2008 in The Proceedings of the National Academy of Sciences, USA. Concerning cardiac hypertrophy, Dr. Koch's group, in a seminal paper published in Science in 1998, were the first to demonstrate that signaling through the heterotrimeric Gq was the common signaling trigger for pressure overload hypertrophy and inhibition of Gq could block both adaptive and maladaptive hypertrophy. The latter study above published in PNAS did indeed show that GRK5's pathological actions in the nucleus of myocytes followed Gq activation.

Finally, Dr. Koch, widely regarded as a leader in cardiac signal transduction, is equally regarded as a leader and mentor of junior investigators. Over 40 Fellows have trained in his lab with several now supported by their own NIH grants in academic medicine. This is a source of great pride as he relishes mentorship and influencing the careers of young scientists.

### *Previous Award Winners....*

**Jeffrey D. Molkentin, Ph.D.**  
(Kyoto, Japan: 2010)

**Mathias Gautel, M.D., Ph.D.**  
(Nice, France: 2009)

**Joseph Loscalzo, M.D.**  
(Toronto, ON: 2006)

**Eric Olson, Ph.D.**  
(New Orleans, LA: 2005)

**Issei Komuro, M.D., Ph. D.**  
(Tokyo, Japan: 2003)