

## ISHR Outstanding Investigator Award

The purpose of this annual 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 \$3,000 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.



**President**  
E Murphy, *USA*

**President Elect**  
T Eschenhagen, *Germany*

**Past President**  
M Avkiran, *UK*

**Secretary General**  
L Delbridge, *Australia*

**Treasurer**  
A Gustafsson, *USA*

**Journal Editor**  
J Solaro, *USA*

**Bulletin Editors**  
L Anderson Lobaugh, *USA*  
T Ruigrok, *The Netherlands*

**Council 2016-2019**  
H Ardehali, *USA*  
M Avkiran, *UK*  
J Backs, *Germany*  
L Delbridge, *Australia*  
F Del Monte, *USA*  
F Di Lisa, *Italy*  
D Eisner, *UK*  
T Eschenhagen, *Germany*  
R Fischmeister, *France*  
A Gustafsson, *USA*  
L Hool, *Australia*  
L Kranias, *USA*  
D Lefer, *USA*  
G Lopaschuk, *USA*  
T Miura, *Japan*  
T Murohara, *Japan*  
E Murphy, *USA*  
S Pepe, *Australia*  
P Ping, *USA*  
Y Saito, *Japan*  
RJ Solaro, *USA*  
Y Takeishi, *Japan*  
KK Talwar, *India*  
T Thum, *Germany*  
M Vila-Petroff, *Argentina*  
R-P Xiao, *China*  
Y Zhu, *China*



International Society for Heart Research

## The Outstanding Investigator Award 2017



Award Winner

**Dr. Xander Wehrens**

**“Calcium Release Unit Defects—Source of Many Cardiac Evils?”**

# Xander Wehrens, MD, PhD

## 2017 Award Winner

New Orleans, Louisiana

Dr. Xander Wehrens obtained his MSc, MD, and PhD degrees from Maastricht University in the Netherlands. During medical school, he worked in a surgical research lab for several years resulting in his Master's thesis on the effects of lower limb ischemia-reperfusion injury on mesenteric microcirculation, which was recognized as the best MSc thesis of the year and resulted in a *summa cum laude* distinction for. In 1998, Dr. Wehrens started his research on the congenital long QT syndrome, an inherited arrhythmia disorder. In 2000, he received the national 'Hippocrates Award' at Leiden University for the best thesis written that year by a medical student in the Netherlands. His MD degree was awarded in 2001 with the distinction *summa cum laude*.

Supported by scholarships from the 'Hein Wellens Foundation' and the 'Three Lights Foundation', Dr. Wehrens spent a year in the laboratory of Dr. Robert Kass in the department of Pharmacology at Columbia University in New York City. Following completion of his medical school clerkships, Dr. Wehrens obtained his PhD degree under the mentorship of Drs. Hein Wellens and Robert Kass. In his thesis, Dr. Wehrens described novel biophysical mechanisms by which human mutations affect the cardiac sodium channel, resulting in lethal arrhythmias. Moreover, his discovery that different disease-causing mutations affect the potential therapeutic effects of some class I anti-arrhythmic drugs represented an early example of precision medicine approaches to the treatment of lethal arrhythmias. His thesis was recognized with the 'CARIM Dissertation Award' for the best Ph.D. thesis.

In 2002, Dr. Wehrens returned to Columbia University in New York for a postdoctoral fellow in the laboratory of Dr. Andrew Marks. Under the mentorship of Dr. Marks, he performed groundbreaking seminal work on the role of ryanodine receptor calcium release channels in heart disease. Work during this time led to the development of a new class of drug molecules for the treatment of heart disease, which are currently under clinical investigation.

Since 2005, Dr. Wehrens has been on faculty at Baylor College of Medicine, starting as an Assistant Professor. He was promoted to tenured Associate Professor (2009) and Full Professor (2011), and became the Juanita P. Quigley Endowed Chair in Cardiology in 2011. His current academic appointments include Professorships in the departments of Molecular Physiology and Biophysics, Medicine (Cardiology), Pediatrics (Cardiology), and the Center for Space Medicine. In 2012, Dr. Wehrens became the inaugural Director of the Cardiovascular Research Institute, an inter-departmental institute with over 450

members that collaborate to develop new comprehensive therapeutic approaches and integrative advances in cardiovascular science and medicine.

Dr. Wehrens is internationally recognized for his pioneering research on cardiac arrhythmias and heart failure. He has authored over 190 peer-reviewed articles in top-tier medical journals. He serves on the editorial board of many international journals including *Circ Res.*, *J Mol Cell Cardiol*, *Heart Rhythm*, *JACC Basic Transl Res* and has given over 160 invited lectures and seminars at international meetings and universities worldwide. He received numerous national and international awards and distinctions, including the International Clinical Research Award from the GlaxoSmithKline Foundation, the Basil O'Connor Starter Scholar Research Award from the March of Dimes Foundation, the Distinguished Young Scholar Award from the W.M. Keck Foundation, and the Established Investigator Award from the American Heart Association. Dr. Wehrens has been elected as a fellow of the Heart Rhythm Society, European Society of Cardiology, American Heart Association, International Society for Heart Research, and as an elected member of the American Society of Clinical Investigation.

Dr. Wehrens' lab is focused on gaining a better understanding of the molecular and cellular basis of cardiac arrhythmias and cardiomyopathies. Dr. Wehrens is currently the principal investigator of three R01 research project grants and one R43 small business innovation grant from the National Heart, Lung, and Blood Institute, and one Established Investigator Award from the AHA. For over a decade, Dr. Wehrens has studied the role of defective intracellular calcium handling in atrial fibrillation (AF). In collaboration with Dr. Dobromir Dobrev, Dr. Wehrens' lab described molecular alterations in the cardiac ryanodine receptor complex (RyR2) in patients and animal models of paroxysmal and permanent AF. In subsequent studies, he demonstrated that reduced binding of protein phosphatases to RyR2 may also contribute to enhanced phosphorylation and aberrant calcium release events. Moreover, Dr. Wehrens published a key study showing that persistent leak of calcium via RyR2 can drive progressive atrial remodeling, a key event in the transition from paroxysmal to more persistent AF types.

Another important contribution to the field has been the demonstration that defects in calcium handling proteins contribute to the development of heart failure (HF). Dr. Wehrens demonstrated a causal role for abnormal RyR2 activity in HF progression. In addition, Dr. Wehrens has performed seminal work on junctophilin-2 (JPH2), a protein critical for the maturation and maintenance of calcium release units in cardiomyocytes.

Dr. Wehrens' team demonstrated that downregulation of JPH2 leads to acute HF. Finally, Dr. Wehrens identified SPEG (striated preferentially expressed protein kinase) as a key molecule that interacts with both RyR2 and JPH2 within calcium release units.

The Wehrens' lab pursues the development of novel therapeutic approaches for arrhythmias and heart failure by targeting intracellular calcium handling. New molecular targets are being identified using human genetics, induced pluripotent stem cells from patients with inherited cardiovascular diseases, transgenic mouse models of heart disease, and adeno-associated viruses for gene therapy experiments. Dr. Wehrens is also a founding partner of Elex Biotech, llc, a start-up company that develops RyR2 modulating small molecule drugs for the treatment of ventricular tachycardia, AF, and heart failure.

Dr. Wehrens is passionate about teaching and mentoring students and junior colleagues. He has mentored over 50 trainees in his lab including 7 undergraduate students, 15 PhD students, and 28 postdocs, many of whom have won awards or moved into faculty positions after their training. Since 2008, he served as the co-director of the Medical Scientist-Training program at Baylor College of Medicine. At Baylor, he received the Fulbright & Jaworski L. L. P. Faculty Excellence Award for Teaching and Evaluation. Dr. Wehrens is also actively involved in several national and international societies. He served on the 'Electrical Signaling, Ion Transport, and Arrhythmias' study section from the National Institutes of Health. He served as a member of the steering committee of the Excitation-Contraction interest group of the ISHR and was a member of the selection committee for the Melvis L. Marcus Award. Dr/Wehrens currently serves as a member of the Board of Directors of the Houston chapter of the American Heart Association. Moreover, he co-chairs the ASCI Young Physician-Scientist Awards committee. Finally, Dr. Wehrens chairs the Heart Rhythm Society's Research Committee, after having served as the chair of the Research Fellowship committee for four years.

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

**Johannes Backs, PhD: 2016**

**Thomas Thum, PhD: 2015**

**Åsa Gustafsson, PhD: 2014**

**Deepak Srivastava, MD: 2013**

**Thomas Eschenhagen, MD: 2012**

**Walter J. Koch, PhD: 2011**

**Jeffrey D. Molkentin, PhD: 2010**

**Mathias Gautel, MD, PhD: 2009**

**Joseph Loscalzo, MD: 2006**

**Eric Olson, PhD: 2005**

**Issei Komuro, MD, PhD: 2003**

**Peter Carmeliet, MD, PhD: 2002**