Peter Harris, M.D., Ph.D.
1923 - 2002

Peter Harris was an influential international statesman in cardiology. A science scholar at King's College, London, UK, Harris trained in medicine at Kings College Hosp., qualifying in 1946. During house appointments at King's and the Brompton Hosp., he obtained his MD in 1951, winning the university gold medal and a PhD in 1955. He was appointed lecturer, in 1957, and reader in medicine, in 1962, at Birmingham University. In 1966, he was appointed the first Simon Marks' Professor of Cardiology at the Cardiothoracic Institute and Director of the Institute of Cardiology, in the Univ. of London.

His career, which was dedicated to exploring the cardiovascular system and the origins of heart disease, can be viewed as three chapters. During the 1950's and early 1960's, he was in the mainstream of research, and used established methods of haemodynamic measurements to explore cardiac output and pulmonary blood flow and the metabolism of the heart muscle. [During]…the second stage of his career …his research into the heart muscle turned to experiments at the cellular and molecular level. In 1970, Harris organized a meeting of …an international study group for research in cardiac metabolism, which resulted in the publication of one of the most influential works on cardiology: *Calcium and the Heart.* The third element to Harris's career involved his fascination with the evolution of the cardiovascular and related systems. In a series of essays in 1983, he traced the way that the origins of clinical heart failure might lie in ancient reflexes. His study of the right ventricle of the heart and the blood flow to the lungs of yaks showed they had adapted genetically to high altitude by eliminating the vasoconstrictor response due to reduction of oxygen.

Away from the laboratory, he was a talented musician and artist, and he showed a leaning toward satirical writing. His wife Francesca survives him.

Excerpted from The Lancet 2003: **361:** 1231.

About the Award…

Created in 1986, this very distinguished Award of international importance is the highlight of each World Congress of the ISHR. It is conferred in recognition of a lifetime of distinguished scientific achievements in the field of cardiovascular research.

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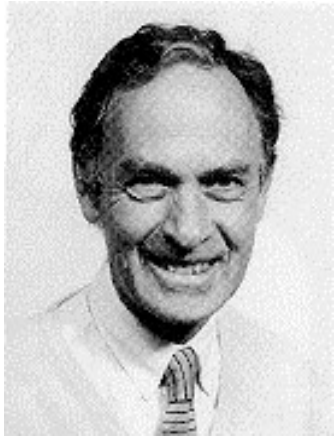
The Peter Harris Distinguished Scientist Award 2015



Peter Harris, M.D., Ph.D.
1923-2002

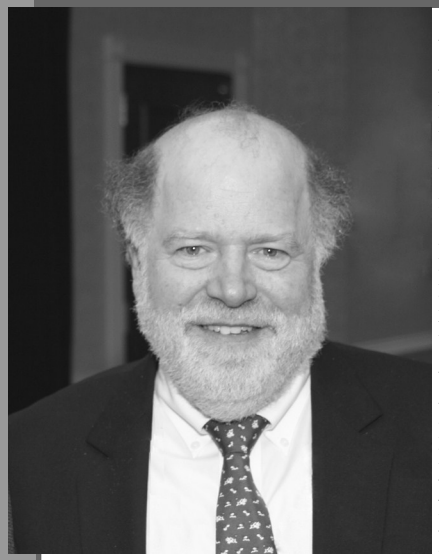
Award Winner

W. Jonathan Lederer, MD, PhD

"X-ROS signaling in Heart"

W Jonathan Lederer, MD, PhD

2015 Award Winner
Bordeaux, France



W. Jonathan Lederer was raised in Honolulu, Hawaii, attended Harvard University as an undergraduate and Yale University for medical and graduate school working with Richard W. Tsien in Physiology for his PhD training. After his medical internship at the University of Washington in Seattle, he received a British-American Heart Fellowship to work with Denis Noble at Oxford University. He is now Director of the Center for Biomedical Engineering and Technology and Professor of Physiology at the University of Maryland School of Medicine in Baltimore, Maryland, USA.

Dr. Lederer has and continues to make fundamental discoveries that change our view of biology and medicine. As a student at Yale with R. W. Tsien, he discovered a Ca^{2+}-activated membrane current that is now known to be the primary membrane current underlying Ca^{2+}-dependent arrhythmias. He and his co-workers then made important discoveries in how protons affect cellular signalling, how Na^+ is linked to Ca^{2+} signalling in excitable cells, how the Na^+/Ca^{2+} exchanger works as an ion transporter and charge carrier, and how the spatial organization of these proteins at the nanoscopic level underlie their signalling. This understanding enabled Lederer, along with Peace Cheng and Mark Cannell, to discover and characterize Ca^{2+} sparks in the heart.

Ca^{2+} sparks, the primary unit of Ca^{2+} release in the heart, are normally triggered by Ca^{2+} influx during the cardiac electrical signal, the action potential, and thus link excitation to contraction. In diverse pathological conditions, Lederer and co-workers also have shown that Ca^{2+} sparks are the essential component of Ca^{2+} leak in the heart that produce Ca^{2+} waves in single cells and arrhythmias in the heart. Importantly, these Ca^{2+} signals underlie the arrhythmogenic current discovered by Lederer as a student.

Lederer and colleagues recently linked Ca^{2+} sparks, the Ca^{2+} leak and the arrhythmogenic current to diverse genetic and acquired arrhythmias. The leak was shown to be due to both Ca^{2+} sparks and the openings of individual SR Ca^{2+} release channels, the ryanodine receptors (RyR2). The Ca^{2+} sparks are produced when a cluster of RyR2 are activated as an ensemble.

Significantly, as this work was unfolding, Lederer and his co-workers also demonstrated that the principles of local Ca^{2+} signalling identified and characterized as Ca^{2+} sparks in heart were a general phenomenon in biology, particularly in muscle. Ca^{2+} sparks are also seen in amphibian skeletal muscle and in vascular smooth muscle, although the function in each tissue was distinct. In vascular smooth muscle, for example, the Ca^{2+} spark and local Ca^{2+} elevation, was shown to underlie vascular relaxation (and not contraction). These discoveries have led to critical new findings on how blood flow is regulated in diverse tissues including the brain (*i.e.* neurovascular coupling). In heart, the Ca^{2+} spark dependent $[Ca^{2+}]i$ transient produce systolic contraction with muscle cell shortening and diastolic relaxation with muscle cell re-lengthening and stretching.

While examining this process, Lederer and co-workers discovered a key new signalling pathway in the heart that links cellular mechanical behaviour to Ca^{2+} signalling. The new signalling pathway, called "X-ROS signalling", is activated by diastolic cellular stretching linked by the cytoskeleton to membrane-bound NADPH oxidase (NOX2) located near the cluster of RyR2 SR Ca^{2+} release channels (within 10's of nanometres). During diastolic filling, microtubules that are linked to NOX2 proteins activate the enzyme which produces local reactive oxygen species (ROS) and this local ROS leads to an increase in the spark rate and thus "tunes" the $[Ca^{2+}]i$ transient. Lederer and his co-workers have thus made surprising discoveries that have fundamentally changed the way we see and think about signalling in biology and medicine.

Dr. Lederer has mentored many individuals who are now leaders in the field, including David Eisner, Shey-Shing Sheu, Mark Cannell, Saleet Jafri, Joshua Berlin, Clive Orchard, Robert Hadley, Godfrey Smith, Colin Nichols, Ernst Niggli, Paulo Kofuji, Hector Valdivia, Heping Cheng, Ana Maria Gomez, L. Fernando Santana, Keith Dilly, Long-Sheng Song, Eric Sobie, Kevin Kit Parker and others. He has mentored individuals with various training & mentoring awards, including recently a K99/R00-award recipient (Benjamin Prosser), multiple NRSA and AHA fellowship recipients. He has had 12 PhD students (two current) and 38 postdoctoral fellows (six current). Dr Lederer has published more than 230 original articles in peer-reviewed journals.

Dr. Lederer is the recipient of numerous honors and awards, including the Harvard College Scholarship (1969); USPHS Scholarship, (1972-1975); Yale Medical School Book Award (1976); M.D./Ph.D. Program, Yale University (1972-1976); British-American Heart Fellow (1977-1979); Established Investigator of the American Heart Association (1981-1986); Councilor (1993-1997), Executive Committee (1996-1998) Biophysical Society; NIH Merit Award (1994-2003); Biophysical Society Cole Award (1998); Wellcome Lecturer (1995, 1999).; Regents Award for Research, University of Maryland, 1999; Founding Fellow, International Society of Heart Research (2001); Fellow of the Biophysical Society (2002). Fred Fay Lecturer (2007), Gordon Moe Lecturer (2007), Isaac Starr Lecturer (2008), Fellow of the American Heart Association (2008), Kirby Lecture (2012), International Chair of Therapeutic Innovation, University of Paris, Lecture (2012), Horowicz Lecture (2012), Lamport Lecture (2012), Dirk L. Brutsaert Lecture (2013), University of Maryland Baltimore Researcher of the Year (2013), and most recently, the ISHR Peter Harris Distinguished Scientist Award (2015).

Past Award Winners

Evangelia Kranias, USA, 2014
Masatsugu Hori, Japan, 2013
James M. Downey, USA, 2010
David J. Hearse, UK, 2007
Arnold M. Katz, USA, 2004
Robert J. Lefkowitz, USA, 2001
Lionel H. Opie, South Africa, 1998
Howard E. Morgan, USA, 1995
Robert B. Jennings, USA, 1992
Albrecht Fleckenstein, Germ, 1989
Setsuro Ebashi, Japan, 1986