

ISHR Research Achievement Award

The purpose of this Award is to recognize a prominent scientist (1) who has a distinguished track record of innovative scientific contributions that have had a major impact on our understanding and/or treatment of cardiovascular disease and (2) who is likely to continue to make major contributions in the future. The main criteria for selecting awardees are scientific excellence and potential for future research contributions. While both the Outstanding Investigator Award (OIA) (awarded annually) and the Research Achievement Award (RAA) recognize established investigators, the OIA is targeted at more junior individuals (at least Assistant/Associate Professor or the equivalent), while the RAA is targeted at more senior individuals (full Professors or the equivalent).

The Research Achievement Award is presented at the triennial ISHR World Congress or, in non-Congress years, at the annual meeting of the ISHR Section to which the winner belongs. The Award consists of a plaque and a monetary prize of \$3,000, which will be used to support the research program of the awardee. An announcement of this Award, along with a photograph and a biosketch, will be published in *Heart News and Views*, and posted in the ISHR website.



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The Research Achievement Award 2015



Award Winner

Dr. Mark Anderson

“Is CaMKII essential for coupling oxidative stress to cardiopulmonary disease?”

2015 Award Winner

Mark Anderson, M.D., Ph.D. Seattle, WA, USA

Mark Anderson is a physician scientist and the William Osler Professor and Director of the Department of Medicine and the Physician-in-Chief of Johns Hopkins Hospital in Baltimore.

Mark graduated from Macalester College with honors in Biology (BA) and from the University of Minnesota with a PhD (Physiology/Pharmacology) and MD (Medicine). He trained in internal medicine, cardiovascular diseases and clinical cardiac electrophysiology at Stanford University. His first faculty position was at Vanderbilt University where he established an independent laboratory and became the Betty and Jack Bailey Professor of Cardiovascular Medicine. At Vanderbilt he directed the training programs in clinical cardiac electrophysiology and cardiovascular diseases and the clinical arrhythmia service. In 2005 he was recruited to the University of Iowa where he first served as Chief of the Division of Cardiovascular Medicine and later as Chair of the Department of Internal Medicine and the Director of the François Abboud Cardiovascular Research Center. In 2014 he was recruited to Johns Hopkins University.

During post-doctoral training at Stanford Mark met Howard Schulman, then Director of the Neurosciences Program, who introduced him to CaMKII; at that time CaMKII was not anticipated to play a role in heart. He was the first to propose the hypothesis that CaMKII was a proarrhythmic signal by promoting aberrant calcium fluxes and membrane hyperexcitability. This hypothesis led to two patents and a series of published manuscripts providing evidence that CaMKII inhibition was antiarrhythmic. The successful application of enzyme inhibitor therapy to arrhythmias was completely unanticipated, challenging the prevailing paradigm that the preferred approach for treating arrhythmias was by ion channel antagonist drugs.

Heart failure patients are at high risk to die suddenly from arrhythmias, but the conjoined clinical phenotypes of mechanical myocardial dysfunction and electrical instability were not known to have a mechanistic connection. Moreover, inotropic therapies for improving myocardial function in heart failure patients increased arrhythmias and sudden death, while ion channel antagonist drugs resulted in high

rates of proarrhythmia and sudden death in heart failure patients. His work (Zhang Nat Med 2005, Erickson Cell 2008, He Nat Med 2011), in collaboration with talented colleagues, showed that CaMKII was a pathological down stream signal for each of the therapeutically validated neurohumoral pathways in heart failure (i.e. beta adrenergic agonist, angiotensin II and aldosterone) and provided a mechanistic framework supporting a view that arrhythmias and heart failure occur together, at least in part, because they are both favored by excessive CaMKII activity. His studies provided important proof-of-concept evidence that CaMKII inhibition reduced heart failure by improving myocardial function while also reducing arrhythmias and prolonging life. These studies led to a patent and various manuscripts from his laboratory and the laboratories of his collaborators. The arrhythmia and heart failure patents were licensed and, together with an emergent scientific literature, contributed to industry efforts to develop CaMKII inhibitor drugs.

CaMKII-related discoveries were greatly accelerated by a Fondation Leducq funded research Alliance for CaMKII Signaling, led by Anderson and co-directed by Dr. Silvia Priori (University of Pavia). This award enabled Anderson and Priori to form an international research network, emphasizing cutting edge research of CaMKII in the cardiovascular system and transatlantic research exchanges. The alliance contributed to training numerous early stage investigators and has produced over 90 publications relating to the role of CaMKII in cardiovascular health and disease between 2009-2013.

While it is widely accepted that excessive oxidant stress is an important upstream signal in many diseases, molecular understanding of critical pathways and successful anti-oxidant therapies have been lacking. Upon identifying CaMKII as an oxidant sensor and a molecular mechanism whereby oxidation induced CaMKII into a constitutively active (i.e. Ca²⁺ and calmodulin-independent) enzyme (Erickson Cell 2008) he developed extensive evidence that excessive oxidant stress contributed to pathological manifestations of myocardial infarction, sick sinus syndrome, diabetic heart disease and asthma by activating CaMKII (He Nat Med 2011, Swaminathan JCI 2011, Luo JCI 2013, Sanders Sci Trans Med 2013).

These studies suggest that CaMKII inhibition may be a successful, but previously unanticipated, anti-oxidant therapy and led to new patent applications. Mitochondria are a critical source of oxidative stress and serve as nodal elements in metabolic adaptation to physiological stress (Wu Nat Commun 2015) and for cell survival decisions (Joiner Nature 2012). Anderson's group is pursuing the hypothesis that CaMKII may exert physiological and disease actions in heart by affecting mitochondrial functions.

Dr. Anderson is a member of the American Society for Clinical Investigation, The Association of American Physicians, The American Clinical and Climatological Association, The Council of the Association of Professors of Medicine, Association of University Cardiologists, a founding Fellow of the Heart Rhythm Society, Senior Fellow of the American Asthma Association and a council member and Fellow of the ISHR. He was an AOA graduate from medical school, an Established Investigator of the AHA and has presented various named lectures.

Mark enjoys spending time with his family, skiing, swimming, running, reading, travel, cooking, music and theater. Anderson is a hopeless musician but last year he started to play the didgeridoo and is learning circular breathing.

Past Award Winners...

Eric Olson, Ph.D.

2013: San Diego, CA, USA

Jeffrey Robbins, Ph.D.

2010: Kyoto, Japan

Martin Lohse, M.D.

2007: Bologna, Italy

Roberto Bolli, M.D.

2004: Brisbane, Australia

Eduardo Marban, M.D.

2001: Winnipeg, Manitoba