

The President's Lecture

In October 2004, the International Council created a new distinguished lecture, named The President's Lecture, which is a highlight of ISHR World Congresses and Section meetings.

The President's Lecture is held at each World Congress of the ISHR and, in non-Congress years, at the annual meeting of one of the 3 largest ISHR Sections on a rotating basis. This lecture is intended to be a high profile event and is scheduled as a keynote plenary lecture. The International Council selects the speaker. **The topic of the lecture is in the field of molecular biology, genetics, genomics or proteomics, but the content should be chosen to be of broad interest to the cardiovascular community.** The speaker is reimbursed for travel expenses, and receives a plaque and a \$1,000 honorarium. A photograph and biosketch of the speaker is published in *Heart News and Views*, and is posted in the ISHR website.

The President's Lecture enhances the content of the ISHR scientific meetings by providing a high-quality presentation in a topical area that is not covered by other distinguished lecture awards, and reflects the continuing growth of the ISHR as a professional Society.

This award is funded by a generous donation from **Roberto Bolli, MD**, Winner of the ISHR 2004 Research Achievement Award, who declined to collect the monetary prize associated with the Award and requested that it be used for this purpose.



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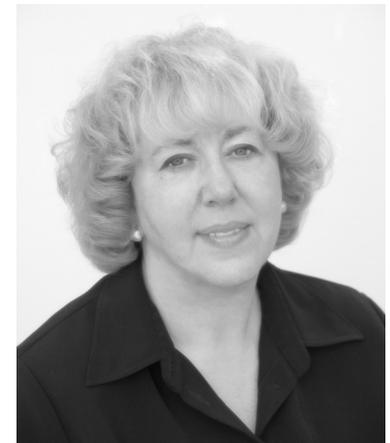
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ISHR

International Society for Heart Research

The President's Lecture 2011



Honored Speaker

Sian Harding, Ph.D.

“Takotsubo Cardiomyopathy
– lessons from a natural
protective mechanism?”

Prof Harding's interests have centred on the function of the cardiac myocyte from the failing human heart since 1987, when she developed a method for the reliable isolation of intact myocytes from human atria and ventricles and established the suitability of the myocyte preparation (both human and animal) for constructing concentration-response curves to pharmacological agents.

Since that time, she has defined the main contractile deficits in myocytes from failing human heart, showing that the frequency response is lost and that stimulation through the betaAR is depressed through Gi-dependent mechanisms. Prof Harding was among those providing evidence for a role of SERCA2a loss and Gi up-regulation in these phenomena. Studies on animal models of betaAR desensitisation or overexpression, hypertrophy and heart failure, as well as adenoviral/AAV transfection of animal myocytes *in vitro* and *in vivo*, have unravelled processes underlying the alterations seen in human cells.

With Dr Roger Hajjar and Federica del Monte (a former Ph.D. student) at Harvard Medical School, she collaborated in the first studies to increase SERCA2a activity in myocytes from failing human heart, by adenoviral transfection of either SERCA2a itself, or antisense to the inhibitory protein, phospholamban. These studies established that increase of SERCA2a activity was sufficient to restore contractile function in these cells. Further studies showed that this is not a pro-arrhythmic strategy either in human or animal myocytes, or in rat

models of gene transfer. She is now part of the group developing a clinical trial for gene therapy in the UK, in parallel with an ongoing trial in the US, using AAV to transfer SERCA2a to failing human myocardium.

In search of a new model of the human ventricular myocyte, Prof Harding has built a group to study cardiomyocytes derived from human embryonic stem cells (hESC-CM) or induced pluripotent cells (iPSC-CM). She has adapted the methods used for adult myocytes, and has characterised their acute contractile and pharmacological phenotype as well as their response to hypertrophic and cardiotoxic agents. She is developing these cells, which can be maintained for months in culture and easily transfected, as an *in vitro* genotype-specific human cardiomyocyte model for high throughput investigations. She also has initiatives for stem cell implantation in combination with advanced materials.

A continuing interest in the betaAR system in failing human heart led to a major discovery concerning the mechanism of action of the beta-blockers; compounds which are standard therapy in heart failure. Prof Harding showed that these compounds have effects over and above those related to catecholamine blockade, by activation of beta2AR-Gi coupling. Since the clinically-used beta-blockers differ in their ability to traffic the beta2AR through the protective Gi pathway, this finding will be highly relevant for the design and selection of compounds for future use in heart failure. Working with the advanced imaging techniques in Dr Julia Gorelik's laboratory, she recently published new insights into spatial modulation of betaAR signalling in myocytes and its disruption during the development of chronic heart failure.

Prof Harding's current interest is in the syndrome of Takotsubo or Stress Cardiomyopathy, in which acute severe heart failure follows a natural or iatrogenic adrenaline stimulus. The particular anatomical and epidemiological features of this, together with its relatively benign outcome compared to acute coro-

nary syndromes, has led her to hypothesize an involvement of protective beta2-Gi coupling. Her lecture will describe *in vivo* and *in vitro* animal models to investigate this syndrome and draw parallels with the protective effects of beta-blockers in chronic heart failure.

Dr. Harding is Professor of Cardiac Pharmacology at the National Heart and Lung Institute, Imperial College, London, and Past-President of the European Section of the ISHR.

Previous Award Winners.....

Dr. Issei Komuro Kyoto, Japan, 2010

"A novel molecular mechanism and regeneration therapy for heart failure"

Dr. R. John Solaro Baltimore, MD, 2009

"Integration of Cardiac Sarcomeric Control Mechanisms with EC Coupling and Metabolism"

Dr. Gerd Hasenfuss Yokohama, 2008

"Stem Cells for Cardiac Regeneration - Dream or Therapeutic Option"

Dr. Jeffrey Robbins Bologna, 2007

"Genetic Manipulation of the Mammalian Heart: What Have We Learned?"

Dr. Mark Sussman Toronto, 2006

"Akt/PKB and Me: Our Nuclear Relationship"