

Janice M. Pfeffer, Ph.D.

1943-2001

The Janice M. Pfeffer Lectureship recognizes the scientific contributions of one of the pioneers in the field of cardiac remodeling. Born in Rockford, Illinois on October 31, 1943, Janice Marie Sikorski graduated with honors from Rockford College. There she studied with a lab partner named Marc Pfeffer, who shared her passion for integrative physiology. Janice and Marc became inseparable not only as husband and wife, but also as collaborators in integrative physiology. Janice M. Pfeffer was awarded her Ph.D. in Physiology and Biophysics from the University of Oklahoma, where she studied under Dr. Edward D. Frohlich. Her doctoral thesis, "Longitudinal Changes in Cardiac Function and Geometry During the Development of Left Ventricular Hypertrophy in the Spontaneously Hypertensive Rat," became a classic study on the role of cardiac hypertrophy and left ventricular remodeling. She continued her studies as a post-doctoral fellow in Dr. Eugene Braunwald's laboratory at the Peter Bent Brigham Hospital, Harvard Medical School. There she demonstrated that progressive ventricular enlargement, "ventricular remodeling", occurs following a myocardial infarction, and that this process continues long after the histologic resolution within the infarct zone. Her landmark study, "Influence of Chronic Captopril Therapy on the Infarcted Left Ventricle of the Rat", definitively demonstrated that ventricular enlargement was attenuated by angiotensin converting enzyme inhibitors, and that favorable alterations in ventricular remodeling in the animal model were associated with improved cardiac performance and prolonged survival. These pioneering animal studies introduced the concept of ventricular remodeling as a potential therapeutic target, and subsequently served as the basis for the landmark clinical trial, Survival and Ventricular Enlargement (SAVE), which showed that long-term treatment with an angiotensin converting enzyme inhibitor (captopril) prevented cardiac remodeling and resulted in improved clinical outcomes in humans. Based upon the results of this seminal translational study, angiotensin converting enzyme inhibitors have become one of the mainstays of therapy for the treatment of myocardial infarction.

In addition to being a meticulous and thoughtful scientist, Janice M. Pfeffer was a devoted mother and wife, who serves as a role model for countless women scientists. The intent of the Janice M. Pfeffer Lectureship is to acknowledge not only the latest insights and advances in the field of cardiac remodeling, but also to remember the remarkable personal and professional qualities that were emblematic of Dr. Janice M. Pfeffer.

About the Award...

Each year, the International Council selects a speaker to deliver the Pfeffer Distinguished Lecture at the World Congress or at the annual section meeting of one of the three largest ISHR Sections. The purpose of this lecture is to honor the memory of Dr. Pfeffer and to recognize her contributions to cardiovascular research. The topic of the lecture must be in the field of remodeling, heart failure and/or hypertrophy. The speaker receives a plaque and \$1,000. honorarium in addition to travel expenses.



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ISHR

International Society for Heart Research

The Janice Pfeffer Distinguished Lecture 2013



Janice M. Pfeffer, Ph.D.
1943-2001

Honored Speaker:

Joan Heller Brown, Ph.D.

"Gq and RhoA Signaling in Cardiac Hypertrophy, Heart Failure and Protection"

2014 Honored Speaker

Joan Heller Brown, Ph.D.

Barcelona, Spain



Dr Joan Heller Brown is a Phi Beta Kappa graduate of Cornell University, where she earned her B.A. degree in Neurobiology. She received her Ph.D. in Pharmacology at the Albert Einstein College of Medicine and completed postdoctoral studies in the Department of Pharmacology at the University of Colorado. In 1975 she

moved to the University of California San Diego (UCSD) as a Research Assistant Professor and has since risen to the rank of Distinguished Professor. In 2005 she was selected following a national search to serve as Chair of the Department of Pharmacology in the UCSD School of Medicine.

Dr Heller Brown was the recipient of a Faculty Development Award from the Pharmaceutical Manufacturer's Association and of an Established Investigator Award from the American Heart Association (AHA). She is an elected Fellow of the AHA, of the International Society for Heart Research, and of the APS Cardiovascular Section. Her awards include the Louis S. Goodman Lecturer, the Lucchesi Distinguished Lectureship in Cardiac Pharmacology, the PhRMA Foundation Award in Excellence, the Albert Einstein College of Medicine Distinguished Ph.D. Alumna Award and the Distinguished Achievement Award from the Basic Cardiovascular Sciences Division of the AHA. She has served on the Scientific Advisory Board for a number of biotechnology and pharmaceutical companies and on the editorial and advisory boards of numerous journals including the *Journal of Biological Chemistry*, *Circulation*, *Circulation Research*, *Molecular Interventions* and *Nature Reviews Drug Discovery*.

An active member of the American Society for Experimental Therapeutics, she served for 5 years as an editor of their flagship journal, *Molecular Pharmacology*.

Dr. Heller Brown's research has focused on signal transduction from G-protein coupled receptors (GPCRs) to cellular responses. She has made multiple important contributions to our understanding of the molecular and physiological actions of dopamine, acetylcholine, catecholamines, thrombin and lysophospholipids on GPCRs and their effectors. These include her seminal finding that muscarinic cholinergic receptor stimulation decreases cAMP production in the heart and that adrenergic receptors regulate phosphoinositide hydrolysis and hypertrophic signaling in cardiomyocytes. Other work from her laboratory established that Gq-coupled receptor signaling activates an array of downstream pathways that contribute to hypertrophy, cardiomyocyte apoptosis, mitochondrial dysfunction and heart failure development. Her studies using CaMKII transgenic and knockout mice have demonstrated a critical role for this protein kinase in Gq signaling and the transition from hypertrophy to heart failure in response to pressure overload. Recent work on ischemia reperfusion injury further elucidated a role for CaMKII in activating NFkB in cardiomyocytes and thereby contributing to inflammation and infarct development. Signaling pathways activated by GPCRs for lysophospholipids such as S1P protect the heart from ischemia reperfusion injury and her laboratory's recent studies used transgenic and knockout mice to demonstrate that activation of the small G-protein RhoA regulates a novel pathway for stimulating protein kinase D (PKD), protecting mitochondria from oxidative stress and hearts from ischemic injury. Dr. Heller Brown's cumulative work spans from fundamental aspects of molecular, biochemical, and genetic analysis to integrative physiology at the whole animal level and has been fundamental for delineating the short and long term consequences of cardiac signaling through G-protein coupled receptors.

Dr. Heller Brown has maintained a continuous high level of extramural grant support for her research program. She has regularly published papers of high impact in prestigious journals in her field including the *PNAS*, *Circulation Research*, the *JCI* and *Science Signaling*. Her 220 papers and review articles are widely cited and she has also contributed chapters to several textbooks including *Basic Neurochemistry*, *Goodman and Gilman's Pharmacological Basis of Therapeutics* and Braunwald's *Molecular Basis of Cardiovascular Disease*. Dr. Heller Brown has been invited to speak at many international meetings, often as a keynote or highlighted speaker. Her work has stimulated that of multiple laboratories working on Gq, RhoA, or CaMKII signaling, and the involvement of CaMKII in arrhythmogenesis, mitochondrial integrity, inflammation and heart failure development has spurred interest in CaMKII as a therapeutic target.

Dr. Heller Brown has been an open and generous collaborator and her collegial approach has enriched the work of others and of the cardiovascular research community. She is also a dedicated mentor, having trained scores of graduate students, served as chair of UCSD's Biomedical Sciences Graduate Program and, for the past decade, served as Principal Investigator on the Department NIH funded Pharmacological Sciences Training grant. Her mentorship has motivated many postdoctoral fellows and junior faculty to develop careers in cardiovascular pharmacology. She is truly an outstanding role model for all scientists, women in particular, and acknowledges her great fortune in having had extraordinary women scientists as role models to inspire her own career.

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