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.
Tom Force grew up in rural Illinois. He graduated from Harvard College where he was inducted into the Phi Beta Kappa Society. After taking a year off to be stage manager for rock concerts at Boston Garden and other venues in and around Boston, he went to Harvard Medical School. He did his residency at the University of Vermont and then his cardiology fellowship at West Roxbury VA Medical Center in Boston. In addition to his clinical responsibilities, he was one of the first of a small handful of investigators who helped develop the field of contrast echocardiography in the early 1980’s. He moved to Massachusetts General Hospital in 1985 to run the Preventive Cardiology Program as well as being Director of the Stress Testing Laboratories, and it was at MGH that he met three scientists who radically changed his direction—John Kyriakis who was working in the Diabetes Unit under Joseph Avruch, and Joseph Bonventre. These three introduced him to basic science, specifically protein kinases, and this quickly became the focus of his work. After Kyriakis and Avruch cloned the JNKs, Force and Kyriakis set out to identify kinase pathways, initially focusing on Raf-1. They showed that Raf-1 was activated by various mitogens, and that it signaled to ERKs via a MAPKK (MEK1/2) which they purified and characterized, thus completing the first mammalian protein kinase cascade (JBC 1993; PNAS 1994). Then, working with Celia Pombo (Dr. Force’s post-doctoral fellow) they identified and characterized mammalian members of the Sterile20-like kinase family (Mst family/MAP4Ks) including Germinatal Center Kinase which is a key regulator of JNKs and p38 activation in systemic inflammation (Nature 1995) and SOK-1/STR25 (EMBO J 1996; JBC 1997) which is a cell death kinase activated by oxidant stress and ischemia. This kinase is mutated in patients with cerebral cavernous malformations, the most common cause of cerebral hemorrhage, and mechanisms potentially underlying this phenotype were later defined (J Cell Sci. 2010). Furthermore, this group was the first to report activation of JNKs by ischemia (JBC 1994).

Around this time, Force began to collaborate with a group of investigators at the Cardiovascular Research Center at MGH, including Tony Rosenzweig and Roger Hajjar, who helped change his direction toward more translational research focusing on the heart, specifically the role of kinases in ischemic injury and pathologic hypertrophy. Force was greatly aided by what would become a long-standing collaboration with James Woodgett at the University of Toronto. Woodgett had initially purified and cloned GSK-3 in Philip Cohen’s lab, and Force and Woodgett began to actively collaborate. They reported the role of GSK-3β in regulating pathologic hypertrophy in The Journal of Cell Biology (2000) and implicated NF-ATs in the process. Force and Woodgett would go on to publish numerous papers exploring the role of GSK-3s in the adult and developing heart. These studies identified central roles of this family of kinases in everything from proliferation/differentiation of embryonic stem cells to cardiac development (deletion leading to double outlet right ventricle, VSD, and a hyperplastic myopathy that led to near obliteration of the LV cavity), post-MI and post-TAC remodeling, ventricular rupture, β-adrenergic responsiveness, and proliferation of cardiac stem/progenitor cells and immature cardiomyocytes (JCI 2008; Circ Res 2010; JCI 2010). During this period, Force also explored the role of Wnt signaling in the heart in the setting of TAC (Mol Cell Biol 2006) and first reported activation of Wnt pathways downstream of traditional GPCRs (PNAS 2003).

Most recently he has played a key role in highlighting the issue of cardiotoxicity of the so-called “targeted therapeutics” which largely inhibit various protein kinases that drive cancer progression. These agents had been predicted to be relatively free of cardiotoxicity, but Force dispelled that myth with the first report of cardiotoxicity with one of these agents (Nat Med 2006), and went on to identify the mechanism. This work increased scrutiny of these agents and culminated in the identification by Ming Hui Chen and Force of very significant cardiotoxicity with sunitinib, an agent widely used in various solid tumors (Lancet 2007). This, and work by a small group of others in 2006-2007 helped launch the concept of a medical sub-speciality called Cardio-Oncology, and also led to the development of guidelines for treating patients with these agents from the Heart Failure Association of the ESC and the U.S. National Cancer Institute, committees on which Force sat. Clearly, identifying potentially problematic agents before they are used in patients is a critical issue and most recently, Force has explored the use of zebrafish as a pre-clinical tool to attempt to do just that (Circ Res 2011).

Recently, Force was named incoming President of the Heart Failure Society of America. He also serves on numerous committees for the American Heart Association. Finally, Force would like to thank all the other collaborators and friends who have supported him, and most of all to thank the students, post-doctoral fellows, and technicians who actually performed the work. Without them, none of this work would have been possible. Force would also like to thank his wife and children for their support and encouragement.

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