ISHR Outstanding Investigator Award

The purpose of this annual award is to recognize an outstanding scientist who (i) is making major and independent contributions to the advancement of cardiovascular science, and (ii) is leading a growing research program likely to play a major role in the future. The main criteria for selecting awardees are scientific excellence, independence, and potential for future research contributions. While the Peter Harris Award recognizes lifelong accomplishments and the Richard Bing Award recognizes young investigators, the Outstanding Investigator Award (presented annually) is targeted at established investigators who are in the intermediate phase of their academic career.

In non-Congress years, the Outstanding Investigator Award is presented at the meeting of the ISHR Section to which the winner belongs. The winner presents a major lecture and receives a $3,000 honorarium and a plaque. An announcement of this Award is published in Heart News and Views, and posted in the ISHR website. The winner receives free registration and reimbursement for travel expenses (up to a maximum or $1500 when the recipient delivers the lecture at his/her local Section meeting, and $3,000 when inter-continental travel is required).

Nominations for the Outstanding Investigator Award are sought by the Secretary General from members of the International Council, members of the Editorial Board of the Journal of Molecular and Cellular Cardiology, and the Councils of ISHR Sections. In addition, the Secretary General publishes an open invitation in the ISHR Website for members to submit nominations.

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The Outstanding Investigator Award 2017

Award Winner
Dr. Jolanda van der Velden
“Bench to Bedside Stories of Sarcomeric Cardiomyopathies”
Dr. Jolanda van der Velden studied Medical Biology in the Netherlands, at the University of Leiden. The main focus of her research involves investigation of changes in sarcomere protein composition and function, which contribute to impaired cardiomyocyte function in heart failure and may be a target for drug therapy. During her PhD, she initiated studies on the role of sarcomere proteins in dysfunction of the failing heart. She optimized and developed several assays to study isoform composition and the phosphorylation pattern of cardiac tissue. By combining protein analyses with measurements of sarcomere force characteristics and ATP consumption in several models of heart failure, her research contributed to a better understanding of the sarcomere protein changes that underlie cardiac dysfunction.

During her PhD studies, she gained expertise with single cell measurements with Rick Moss at the University of Wisconsin, Madison. Since human cardiac tissue is scarce, she optimized the mechanical isolation of single cardiomyocytes and sensitive protein analysis methods. This enabled her group to perform multiple assays on small human biopsies. She defended her PhD thesis, entitled “Correlation between contractile protein composition and energetic and mechanical properties of the heart,” in 1998. Her PhD thesis was awarded the prestigious Hamburger award of the Dutch Physiology Society, named after the Dutch Physiologist Hartog Jacob Hamburgcr. In collaboration with Dirk Duncker (Erasmus Medical Center, Rotterdam), she studied effects of myocardial infarction (MI) and aortic stenosis (AoS) on cellular function in pig and mouse models. Their current collaboration focuses on the effects of diabetes and kidney dysfunction on the heart.

In following years, she developed a method in which one specific myofilament protein is exchanged in single human cardiomyocytes without altering other proteins, a project which was funded by a VENI innovation award (2002) of the Netherlands Organization of Sciences (NWO). This exchange method offers the unique possibility to identify the individual contributions of myofilament proteins to human myocardial performance under (patho)physiological conditions. These innovative studies in single human cardiomyocytes provide a unique niche in human cardiac research. Together with Jennifer van Eyk and Anne Murphy (Johns Hopkins, Baltimore), she has studied the role of site-specific troponin I phosphorylation using the protein exchange method in single human cardiomyocytes. Mass spectrometry analysis revealed a new phosphorylation site on troponin targeted by PKCalpha in human myocardium.

The protein exchange method is also applied in Amsterdam to study the role of mutant sarcomere proteins in inherited cardiomyopathies. With the aid of European funding (FP7 Big Heart consortium) and a VIDI innovation award (2009), her group has shown that mutant proteins impair cardiac function and increase energy utilization of heart contraction. Basic studies in cardiac tissue from cardiomyopathy patients are combined with cardiac imaging studies in collaboration with Cardiology departments in the Netherlands. These in vivo imaging studies in asymptomatic individuals who carry a sarcgolome mutation revealed that the energetic deficit is already present before the heart remodels. Based on these studies, van der Velden and colleagues aim to initiate a pilot clinical trial with metabolic therapy in mutation carriers without cardiac hypertrophy. Currently, her group explores the effects of mutant proteins in combination with mitochondrial and energetic perturbations in the heart. In a recently funded national research consortium (2015), coordinated by van der Velden, the role of genetic and environmental factors in cardiomyopathy development is studied.

Together with Michiel Helmes (Ionoptix) and Davide Iannuzzi (Physics, Vrije Universiteit, Amsterdam), she developed a method to measure force-length relations in intact cardiac muscle cells. This method was recently published in Cardiovascular Research, and the optimized Ionoptix set-up is used by many colleagues throughout the world. The joint effort of physiologists and physicists was essential to achieve the technological advance needed to optimize the Ionoptix set-up. The single cell system is an example of a fruitful collaboration between academia and industry as acknowledged by the VSNV (associations of universities in the Netherland, http://www.vsnv.nl/volorisatie-in-beeld/vrije-universiteit.html). This novel cell system paves the way for a whole new class of drug tests and physiological studies.

A major observation identified using the single cell method was a defect in relaxation of the failing human heart. During her PhD studies, she proposed that altered properties of the sarcomeres underlie diastolic dysfunction of the end-stage failing heart via an increased sensitivity of myofilaments for calcium. She showed that secondary disease-related post-translational protein changes (phosphorylation, degradation) underlie impaired relaxation of failing human heart muscle. Importantly, together with colleagues from Amsterdam (Ger Stienen, Walter Paulus) and Debrecen (Attila Borbely, Zoltan Papp), she demonstrated that high passive stiffness of sarcomeres could contribute to high end-diastolic pressure in heart failure patients with preserved ejection fraction (HFpEF patients). This observation formed the basis for many studies in human and animal HFpEF models and the discovery that altered phosphorylation of titin is the cause of high cardiomyocyte passive stiffness. Modulation of the signalling pathway regulating titin phosphorylation may represent a way to treat HFpEF patients.

She has trained many PhD students and post-docs, many of whom continue onto a successful career in academia. As a biologist, with training in physiology and cell biology, she aims to build a bridge between basic laboratory studies and clinical studies. In 2013, she became Netherlands Heart Institute professor on “Cardiovascular Pathophysiology of Cardiomyopathies,” which enables her to stimulate translation research projects at a national level. As chair of the Physiology department (since 2014), and director of the cardiovascular research institute in Amsterdam (since 2014; since 2016 director of the Amsterdam Cardiovascular Sciences Institute together with Mat Daemen), she is in the unique position to execute translational research programs to study pathomechanisms from bench to patient by combining in vivo cardiovascular imaging with novel methodologies to study both muscular and vascular cellular properties of the heart.