

ISHR Outstanding Investigator Prize

The purpose of this Prize is to recognize an outstanding scientist who (i) is making major and independent contributions to the advancement of cardiovascular science, and (ii) is likely to further develop his/her research 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 life-long accomplishments and the Richard Bing Award recognizes young investigators, the Outstanding Investigator Prize is similar to the Research Achievement Award; the major difference between the two is that the latter is presented during the ISHR World Congress while the former is given at Section meetings. To avoid overlap with the Research Achievement Award, the Outstanding Investigator Prize is not given in the years when the World Congress convenes.

The Outstanding Investigator Prize is presented at the meeting of the ISHR Section to which the winner belongs. The winner receives free registration, reimbursement for travel expenses, \$3,000 honorarium and a plaque. An announcement of this Prize, along with a photograph and a biosketch, is published in the *Journal of Molecular and Cellular Cardiology* and in *Heart News and Views*, and posted on the ISHR website.

Nominations for the Outstanding Investigator Prize 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 *JMCC*, in *Heart News and Views*, and on the ISHR Website for members to submit nominations.

This award is funded by a generous contribution from Aventis Pharmaceuticals.



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ISHR

International Society for Heart Research

The Outstanding Investigator Prize 2006



Prize Winner

Dr. Joseph Loscalzo

Joseph Loscalzo, M.D., Ph.D.

2006 Prize Winner
Toronto, ON

Joseph Loscalzo was born on October 26, 1951, and grew up in New Jersey. He received an A.B. in biochemistry, *summa cum laude*, from the University of Pennsylvania in 1972, and an M.D. and Ph.D. in biochemistry from the same institution in 1978. He then trained in internal medicine and in cardiology at Brigham and Women's Hospital and Harvard Medical School from 1978 through 1984, after which he joined the Department of Medicine at Brigham and Women's Hospital and was appointed Assistant Professor of Medicine at Harvard Medical School. In 1994, he moved to Boston University as Chief of Cardiology, Director of the Whitaker Cardiovascular Institute, and Distinguished Professor of Cardiovascular Medicine. In 1997 he was appointed Wade Professor and Chair of the Department of Medicine at Boston University. In July of 2005, he returned to Brigham and Women's Hospital and Harvard Medical School as Physician-in-Chief, Chairman of the Department of Medicine, and Hersey Professor of the Theory and Practice of Medicine.

Dr. Loscalzo has spent his research career focusing on the biology of endothelial nitric oxide, and on redox biochemistry and oxidative stress in cardiovascular health and disease. Beginning in the early 1980s, he first demonstrated a molecular mechanism for the antiplatelet effect of nitric oxide donors, conclusively showing that this action requires the formation of S-nitrosothiols. He went on to show that endothelium-derived relaxing factor exerted its vascular effects, in part, through the formation of this class of biologically active compounds. Furthermore, his group first demonstrated that S-nitrosation of protein cysteinyl residues occurs *in vivo*, representing a form of posttranslational modification of protein thiols, altering protein function and cell phenotype. He went on to establish a novel class of bifunctional pharmacological agents in which a basic pharmacophore is minimally modified to incorporate an S-nitrosothiol moiety and its nitrovasodilator and antiplatelet activities without altering the basic pharmacological action of the parent compound

(*e.g.* S-nitrosocaptopril). In addition, he demonstrated the importance of protein disulfide isomerase as a cell-surface catalyst of trans-S-nitrosation from the extracellular to intracellular environment. Most recently, he has isolated the S-nitrosoproteome from endothelial cells and confirmed that many proteins known to undergo S-nitrosation in isolation comprise major elements of that proteome. Furthermore, he showed that the mitochondrial and perimotochondrial environment is the key compartment for protein S-nitrosation in endothelial cells.

Dr. Loscalzo expanded his investigation of the anti-thrombotic effect of nitric oxide by showing that platelets generate nitric oxide, and that this platelet-derived nitric oxide pool limits the recruitment of platelets to the growing platelet thrombus. In addition, his group conclusively showed that nitric oxide can induce megakaryocyte apoptosis, but when megakaryocytes are pretreated with thrombopoietin, nitric oxide leads to thrombopoiesis, an important, key observation in platelet biology.

Dr. Loscalzo also developed the concept of oxidative enzymopathies, showing that acquired or genetically determined deficiencies of key antioxidant enzymes lead to nitric oxide insufficiency states. His group has demonstrated this key concept in hyperhomocysteinemia, which is associated with an acquired deficiency of glutathione peroxidase-1 owing to the unique effect of homocysteine on translational of this selenocysteine-containing protein; in glucose-6-phosphate dehydrogenase deficiency, which can be either genetically determined or acquired by mild hyperaldosteronism as his group has recently shown, both of which can cause endothelial oxidant stress and dysfunction; and in glutathione peroxidase-3 deficiency, which his group showed is a unique, genetically determined cause of platelet-mediated arterial thrombosis and stroke in young individuals characterized by a dysfunctional promoter haplotype.

Dr. Loscalzo has received many awards in recognition of his accomplishments, including the Distinguished Sci-

entist Award from the American Heart Association, the George W. Thorn Award for Excellence in Teaching at Brigham and Women's Hospital, Educator of the Year Award in Clinical Medicine from Boston University, the Glaxo Cardiovascular Research Award, election to the American Society for Clinical Investigation, and election to the Association of American Physicians. He has served on several NIH study sections and editorial boards, and has chaired the Gordon Conference on Thrombolysis. He served as Director of the National Institutes of Health-sponsored Specialized Center of Research in Ischemic Heart Disease at Boston University for 10 years, an associate editor of the *New England Journal of Medicine* for nine years, Chair of the Cardiovascular Board of the American Board of Internal Medicine, Chair of the Research Committee of the American Heart Association, Chair of the Scientific Board of the Stanley J. Sarnoff Society of Fellows for Research in Cardiovascular Sciences, and Chair of the Board of Scientific Counselors of the National Heart, Lung, and Blood Institute of the National Institutes of Health. He is currently Editor-in-Chief of *Circulation*, a senior editor of **Harrison's Principles of Internal Medicine**, and a member of the Advisory Council of the National Heart, Lung, and Blood Institute of the National Institutes of Health.

Previous Award Winners....

Eric Olson, Ph.D.

(New Orleans, LA: 2005)

Issei Komuro, M.D., Ph. D.

(Tokyo, Japan: 2003)

Peter Carmeliet, M.D., Ph.D.

(Szeged, Hungary: 2002)