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 lifelong 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.

The Outstanding Investigator Prize is presented at the meeting of the ISHR Section to which the winner belongs. To avoid overlap with the Research Achivement Award, the Outstanding Investigator Prize will not be given in the years when the World Congress convenes. The winner receives $3,000. and a plaque. An announcement of this Prize, along with a photograph and a biosketch, will be published in the *Journal of Molecular and Cellular Cardiology* and in *Heart News and Views*, and posted in the ISHR website. The winner receives free registration and reimbursement for travel expenses.

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 Councils of ISHR Sections. In addition, the Secretary General publishes an open invitation in *JMCC*, in *Heart News and Views*, and in the ISHR Website for members to submit nominations.

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The Outstanding Investigator Prize 2003

Prize Winner

Dr. Issei Komuro

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

2003 Prize Winner
Tokyo, Japan

Dr. Komuro started his research career by purifying cardiac myosin heavy chain (MHC) isoforms in Dr. Yoshio Yazaki's laboratory at the University of Tokyo in 1985. He first showed differences in the protein structure and enzymatic activity between α and β MHC. Since the discovery of an increase in β MHC in hypertrophied hearts, his research interest has been focused on cardiac hypertrophy. He analyzed altered gene expression in cardiac hypertrophy by two-dimensional gel electrophoresis of *in vitro* translated products and showed that the fetal gene program is reactivated in hypertrophied hearts. Based on the hypothesis that similar mechanisms are involved in cell hypertrophy and proliferation, he examined the expression of protooncogenes during the course of hypertrophy. He also first cloned SERCA2 from the heart and demonstrated its downergulation at mRNA and protein levels in hypertrophied hearts. In 1987, he developed the procedure to stretch cultured cardiomyocytes and extensively studied signal transduction processes involved in the development of cardiac hypertrophy induced by mechanical stress. He first applied molecular biology and biochemistry to analyze the molecular mechanism of mechanical stress-induced biological events.

From 1989 to 1993, he was a postdoctoral fellow in Dr. Izumo's laboratory at Beth Israel Hospital/Harvard Medical School in Boston. He succeeded in isolating the cardiac homeobox protein Csx/Nkx2.5, a transcription factor essential for cardiac development. The discovery of Csx/Nkx2.5 greatly stimulated the study of cardiac development, and Csx/Nkx2.5 has been used worldwide as an early marker of the heart.

After returning to Japan, he isolated human Csx/Nkx2.5 and determined the locus of this gene, which later led to the discovery that Csx/Nkx2.5 is one of the genes responsible for various heart diseases such as atrial septal defect, ventricular septal defect, Tetralogy of Fallot, Epstein anomaly and atrio-ventricular block. He clarified the molecular mechanism of Csx/Nkx2.5 involvement in cardiac development by isolating proteins which associate with Csx/Nkx2.5, and the role of bone morphogenetic proteins in cardiac development by establishing a cardiomyocyte differentiation system. He has also elucidated the role of molecules such as angiotensin II and calcineurin in the development of cardiac hypertrophy and remodeling using transgenic mice. In 2001, he became a professor and chairman of cardiovascular medicine at Chiba University where he leads over 100 doctors in clinical work as well as research.

Dr. Komuro is a pioneer in, and has made great contributions to, the research fields of cardiac hypertrophy and development. His work has provided valuable insights into the pathophysiology of cardiac diseases; for example, elucidation of the molecular mechanism of mechanical stress-induced cardiac hypertrophy and demonstration of the role of angiotensin II in cardiac remodeling provided the rationale for inhibiting the renin-angiotensin system in patients with heart failure. In the future, insights gained from the study of cardiac development will prove to be even more important to the burgeoning fields of gene therapy and regenerative medicine.

Originality is a feature of Dr. Komuro's research and he is also a highly productive man. He has published over 200 original articles, many of which have appeared in leading journals. He has also published 40 book chapters/review articles, is a regular speaker at national and international meetings, and serves as an associated editor of the *Journal of Molecular Cellular Cardiology* and an editorial board member of *Circulation* and *Circulation Research*.

2002 Prize Winner

Peter Carmeliet, M.D., Ph.D. Szeged, Hungary

Peter Carmeliet was born on December 8, 1959. He is married and has 3 children. Dr. Carmeliet graduated from the Univ. of Leuven, Belgium, as M.D. in 1984 and Ph.D. in 1989. His postdoctoral training was in molecular neurobiology at Harvard Medical School (1989-90) and in functional genomics at the Whitehead Institute, M.I.T., MA with Dr. Mulligan (1990-91). He was promoted to the rank of Assoc. Professor in 1994 and of Professor of Medicine at the Univ. of Leuven in 2000. In 1995, he became vice-director of the Center of Transgene Technology and Gene Therapy in Leuven. Dr. Carmeliet has been appointed Visiting Professor of Medicine at the Univ. of Brussels (1995-97), Professor of Medicine at CARIM, Univ. of Maastricht, Netherlands (2000-now), and Visiting Professor at the Univ. of Darmouth, NH (2003).

Formation of blood vessels ("angiogenesis") is the main theme of Dr. Carmeliet's research. During his stay with Dr. Mulligan at M.I.T., he used novel gene technologies to generate mice lacking each component of the plasminogen system and many components of the coagulation system, thereby being the first to generate a proteinase deficient mouse model. These studies led to novel insights into the role of plasminogen in angiogenesis and various cardiovascular disorders including hemostasis, atherosclerosis, restenosis, aneurysm formation, pulmonary and systemic hypertension, and cardiomyopathy. The phenotyping of these models required the use of biochemical, histological and physiological techniques, adapted to the small size of the mouse model.

In 1996, Dr. Carmeliet published a landmark study documenting the critical role of the vascular endothelial growth factor (VEGF) in embryonic angiogenesis. Recently, he demonstrated that lack of particular VEGF isoforms increased the risk of developing congenital cardiovascular malformations as found in DiGeorge patients. In addition, he characterized the enigmatic role of placental growth factor (PlGF), a family member of VEGF, and demonstrated that PlGF treatment promotes revascularization of ischemic tissue, while delivery of its receptor antagonist blocks cancer and several other angiogenic inflammatory disorders. The biopharmaceutical industry has expressed interest in the potential use of these promising preclinical findings in clinical testing. Dr. Carmeliet's meticulous phenotypic analysis of additional gene-targeted mice led to the unpredicted finding that loss of HIF-2a (a hypoxia-inducible factor) and inhibition of VEGF impair lung maturation *in utero*, while treatment with VEGF prevents fatal respiratory distress in premature mice. He also found that VEGF is a modifier of motoneuron degeneration in mice and in patients with amyotrophic lateral sclerosis - a finding which provides unexpected insight into the enigmatic pathogenesis and raises hope for treatment of this fatal disorder. Outside of the angiogenesis field, he developed transgenic mice models for long QT3 cardiac arrhythmia, endochondral bone formation and Zellweger syndrome.

Dr Carmeliet's scientific research, translating genetic and molecular insights into novel therapeutic opportunities, is of excellent quality and he has published numerous original articles, reviews and editorials in leading journals. He has gained a worldwide reputation as a researcher and a lecturer, and he is frequently invited to deliver plenary lectures at international meetings. He is the recipient of honorary memberships and several awards, including the Liliane Bettencourt Award Life Sciences (2003), Francqui Prize (2002), and Bristol Myers Squibb Grant (2001). He has served on the Advisory Boards of the Max Planck Institute, the Wellcome Trust, Cancer Research Institute Lausanne, and Int'l Cancer Research Treatment Torino, on the Editorial Boards of *Cancer Cell*, *Circulation Research*, *Trends Cardiovascular Medicine*, and as Guest Editor of *Cardiovascular Research*.