ISHR Outstanding Investigator Award

The purpose of this 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 $5,000 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 2009

Award Winner

Dr. Mathias Gautel

Mathias Gautel, M.D., Ph.D.

2009 Award Winner
Nice, France

Mathias Gautel was born in 1963 in Karlsruhe, Badenia (Germany) where he grew up. He studied Medicine at Heidelberg University, Germany, graduating in 1991 with an MD "summa cum laude". During his medical studies, he commenced research on the giant muscle protein titin, for which he obtained the first cDNA clones in 1988. He subsequently continued to pursue research on titin at the European Molecular Biology Laboratory in Heidelberg, first as a Postdoctoral Fellow of the German Research Foundation (DFG) and then as an independent team leader with a Habilitation Fellowship of the DFG in the Structural Biology Division. Dr. Gautel obtained his Habilitation (MD PhD equivalent) in Biochemistry from the Medical Faculty of Heidelberg University in 1996. In 1998, he was awarded a Heisenberg Fellowship, the highest award of the DFG for young independent scientists, to work at the Max-Planck Institute of Molecular Physiology in Dortmund. Since 2002, he has been Professor of Molecular Cardiology at King's College London, where he was awarded a British Heart Foundation Chair in 2008.

Dr. Gautel's research centres on the analysis of striated muscle proteins involved in cytoskeletal assembly and signalling, and their involvement in heart disease. His contributions towards elucidating the basic molecular architecture of the giant protein titin, its interactions with other sarcomeric proteins (several of which he has discovered), and their regulation, atomic structure and biomechanics, have significantly furthered our understanding of the involvement of the titin protein network in human muscle diseases. Dr. Gautel's work has made seminal contributions to the understanding of the protein interactions of titin in the sarcomeric Z-disk, A-band and M-band, with his discovery of length-adjusting elements in Z-disk titin and new proteins interacting with Z-disk and M-band titin allowing reconstructions of the molecular layout of these structures. The discovery of the giant protein obscurin in his laboratory has led to a new paradigm in muscle cell biology and has opened up the novel field of proteins with multiple sarcomeric localisation at Z-disks and M-bands. The crucial role of obscurin in M-band assembly was underscored recently by his discovery of a ternary complex of titin, obscurin and the M-band protein myomesin; this complex is disrupted in two different hereditary myopathies with mutations in titin. Dr. Gautel's pioneering contributions to titin single molecule analysis unravelled the molecular mechanism of muscle passive elasticity, and recently, of the mechanoenzymatics of the titin kinase domain. Through a long-standing structural, biochemical and cell biological effort devoted to the signalling functions of the protein kinase domain of titin, his work has led to the novel concept of a mechano-regulated protein kinase that is implicated in load dependent protein turnover in muscle. He has identified a new signalling pathway emanating from the titin kinase domain, and shown that this is disrupted in a hereditary myopathy with titin mutation. His recent work has revealed, for the first time, how a protein kinase can be activated by mechanical strain. This new paradigm of kinase mechanosignalling may be relevant to a large number of cytoskeletal protein kinases that have been implicated in cardiovascular regulation.

Dr. Gautel's identification and analysis of the primary sequence of cardiac myosin-binding protein-C (cMyBP-C) has led to the discovery that this gene was responsible for chromosome 11-linked hypertrophic cardiomyopathy, now realized to be the most commonly affected gene in this disease. Investigations in his laboratory have revealed how cMyBP-C interacts with titin and myosin, and how phosphorylation of a specific domain contributes to the regulation of cardiac contraction. Dr. Gautel was the first to identify and characterize the phosphorylation of cMyBP-C at the molecular level, to delineate its structural and regulatory interactions, and to realize its involvement in familial hypertrophic cardiomyopathy.

Dr. Gautel has published numerous papers in the foremost biomedical journals, and through implementation of his basic research findings, has been able to elucidate the molecular mechanism of disease-associated mutations in myosin, myosin-binding proteins and titin. His work has combined, in a rare manner, cellular, molecular and structural approaches with a profound interest in disease mechanisms. The pioneering work of Dr. Gautel in muscle research and his continued scholarly contributions are also reflected by his long-standing service on the funding committees of international agencies in France and the United Kingdom. He is associate editor of the Journal of Muscle Research and Cell Motility.

Previous Award Winners....

Joseph Loscalzo, M.D.
(Toronto, ON: 2006)

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)