The historical city of Kyoto, Japan hosted the XX World Congress of the ISHR. This was a welcome return to Japan for the World Congress, after an 18 year absence since the Kobe meeting in 1992. Organized by the President of the ISHR, Prof Matt Hori, and his colleagues, the meeting theme was ‘Paradigm Shift to Integrated Cardiology – Gene, Function and Life’. For many of us, this was our first time visiting Japan, and we were fortunate to combine a highly stimulating scientific event with such a rich cultural experience. This was immediately evident on arriving at the Kyoto International Conference Center, where the grand hexagonal architecture starkly contrasted with the peaceful water garden setting in which it was nestled. Surely this must have featured in a James Bond/Austin Powers movie at some point in its lifetime?
The meeting consisted of over 200 symposia, interspersed with numerous Special Award Lectures and 3 poster sessions. Symposia themes covered all aspects of cardiovascular research, with lectures given by the leading scientists in their discipline. The scientific program included 50 symposia held throughout the four days of the meeting. Such was the quality and quantity of science on offer, my laboratory colleagues and I had to plan carefully to strategically split up at times to ensure that we could garner all the information we wanted. Award lectures recognized the impact and contribution of the leading investigators in cardiac research, and were held in the suitably immense Main Hall. These commenced with the Keith Reimer Distinguished Lecture, presented by Prof Richard Moss, who gave an intriguing talk on ‘Phenotypic responses due to induced genetic ablation of cMyBP-C in adult mice’. Subsequent lectures were given by Profs Issei Komuro (President’s Distinguished Lecture), Junichi Sadoshima (Janice Pfeffer Distinguished Lecture), Jeffery Molkentin (Outstanding Investigator Award), James Downey (Peter Harris Distinguished Scientist Award), Jeffrey Robbins (Research Achievement Award) and Oliver Smithies (Nobel Laureate Lecture), culminating with the Special Lecture on the final day of the conference by Prof Shinya Yamanaka.

Lunch each day was a pleasant reminder of our Japanese setting, with the beautiful bento boxes providing a refreshing change from the typical sandwich served at most conferences. Hour-long poster sessions were held after lunch, promoting open discussion amongst Society members. These were very well attended, and structure was brought to the sometimes chaotic nature of these sessions, with each presenting author given the opportunity to describe their poster to 2 chairpersons and a set of ‘groupies’. For the first time, a student investigator poster competition was held at the Congress. All posters were assessed by a most diligent panel of judges and Manabu Taneike (Osaka Univ, Japan), Yin Liu (Univ West Ontario, Canada) and Hisayuki Hashimoto (Keio Univ, Japan) were awarded the ISHR International Poster Prize for best poster on each of the three days.

The Congress was truly blessed! I am happy to say that the Congress was a great success with regard to both science and social programs. We had more than 1,300 participants from 44 countries including 412 from Japan; seven hundred investigators presented their work at poster sessions and many of them applied for Poster Awards. Many investigators came together at the poster sessions for communication between young researchers and senior scientists. I am grateful to the Society for supporting more than 100 young researchers with travel awards.

The scientific program was superb with a nice blend of basic and clinical science. The first-class basic research science was incorporated into 23 symposia sponsored by ISHR-International and 11 Section-sponsored symposia. These symposia were perfectly blended with 15 clinically relevant
The importance to the Society of promoting the careers of its younger members was also reflected in the generous travel awards granted, which helped so many make it to Japan, as well as in the two Early Career workshops that were organized. ‘Publishing and its perils’ was the theme of the first session, hosted by Elsevier and the Society’s own Journal of Molecular and Cellular Cardiology, where Dr Elizabeth Murphy and Prof David Eisner gave some invaluable advice on the publication process and recommended strategies to optimize output. This was followed by a workshop discussing the role of mentoring in the development of the Early Career Researcher. Drs Meredith Bond and Thomas Eschenhagen kindly offered their views and advice on many aspects of the mentor/protégé relationship and how this can be exploited to maximize competitiveness in our fields of research. The two workshops proved to be popular sessions with both younger and more senior members of the Society, and hopefully similar sessions will be included in future World Congresses. The support of Prof Hori’s organizing committee and of the ISHR International in staging these workshops was most generous.

The social programs provided an opportunity for Congress participants to touch and feel Japanese culture, and to enjoy warm friendships with new and old acquaintances. The Aoi Festival, the most graceful festival in Kyoto, was a highlight of the social program, and will be a lasting memory for everyone who attended. The banquet in the Swan Garden was also wonderful, cheered by Japanese drum playing. These events were all supported by the excellent weather that we enjoyed during the Congress.

The first-class science, the global human communications and a good blend of new science and old culture—all of these are memorable and impressive. We look forward to seeing all of you again in San Diego in 2013.

Masatsugu Hori
President ISHR

The importance to the Society of promoting the careers of its younger members was also reflected in the generous travel awards that was presented in these programs. The ISHR Award lectures and special lectures by Professors Oliver Smithies and Shinya Yamanaka were also highlights of the Congress. Finally, the Richard J. Bing Young Investigator competition, tutorial sessions and ECR workshops were stimulating programs for young researchers.

The timing of the meeting was organized to coincide with the graceful Aoi Festival. Dating back to the 8th century, the Festival consists of services and rituals, and a procession from the Imperial Palace to the Shimogamo and Kamigamo Shrines. It was a wonderful opportunity to see traditional Heian period dress and gain some further insight into Japanese culture. Other excursions to the numerous shrines dotted around the city were also rewarding, including a visit to the incredible Kiyomizu Temple situated in the hills overlooking Kyoto. Despite the crowds, this was a very peaceful place, with the waterfall and the deep sound of the bells. The Banquet on the final night of the conference opened with an impressive Japanese drum performance. With the sun setting, the buffet and drinks outdoors made for a relaxed social setting and the chance for even some of the most unexpected groovers to do their thing on the dance pontoon.

The gathering of all the sections of the ISHR always ensures that the World Congress is a rich and vibrant scientific outing and a good opportunity to see old friends and colleagues. The meeting in Kyoto certainly proved this, and congratulations go to Prof Hori and his colleagues for organizing a highly successful and convivial meeting. The World Congress now moves across the Pacific to San Diego in 2013, but after our wonderful experience of Kyoto’s science and hospitality, many of us will look for future opportunities to return to Japan to further indulge in its culture and beauty.

Dr James Bell
Melbourne, Australia
1. Delegates enter the Main Hall in the Kyoto International Congress Center for the Opening Ceremony of the Congress.

2. Delegates meet both old and new friends at the opening day Get-together reception in the Grand Prince Hotel.

3. Japanese schoolgirls practice speaking English with (from left) Australians Helena Viola and Livia Hool (Univ W Aus, Crawley, WA, AUS), and JMCC Editor, David Eisner.

4. Secretary General Richard Moss presents an engraved wall clock to outgoing President Roberto Bolli as thanks for his service to the ISHR (Sec Gen 1998-2004; Pres-Elect 2004-2007; Pres 2007-2010).

5. Colorful chopsticks for sale in Kyoto.

6. Delegates were treated to a rousing Japanese drum performance as a prelude to the meeting Banquet.
Dear Colleagues,

This is my first column as President of ISHR-Intl. First of all, I would like to sincerely thank all of the members of the ISHR for the successful World Congress in Kyoto in May. Several months have quickly passed after the World Congress, the hot fever of excitement has now cooled down, and we have returned to our usual research work. Herewith, I would like to consider our research goals as members of the ISHR.

All animals and plants on the earth are alive because of biological activity. The biological activity of living organisms is based on their biological structure, metabolism and function; these three properties can be used to describe whole bodies, organs, tissues and cells - even intracellular organelles. Structure, metabolism and function are closely related to each other, and compose a triangular complex or ‘unit of life’ (Figure). Structure is visible, whereas function and metabolism are not visible; however, function can often be recognized as a structural change if carefully watched, and metabolism may also be detected as heat or body temperature.

The triangle formed by the three axes, structure, function and metabolism, also applies to the heart. The heart is mainly recognized as a pump that delivers blood to the whole body and organs. Engineering theories and technologies such as mechanical engineering and fluid dynamics have been used to analyze this mechanical function of the heart. A number of physical parameters and indices (e.g. pressure, volume, velocity, dP/dt max, Vmax, Emax), and various formulas (e.g. La Place’s law and Bernoulli’s theorem), have been used to describe the various phenomena and function of the heart. The heart functions not only as a mechanical pumping machine, but also as a secretor of hormones (e.g. natriuretic peptides, ANP and BNP). The heart is also a sensing organ for venous return with afferent vagal nerve signals to the brain. Thus, the heart is not simply a machine.

In terms of structure, the heart is basically a sac of blood. The four chambers of the heart have their own valves to control the direction of the bloodstream like a classic water pump. The macroscopic structure of the heart has been precisely observed by cardiologists with the aid of echocardiography, computer tomography and MR imaging techniques. With these technologies, we can also observe the dynamic blood flow in the heart and vessels of individual patients with cardiac diseases.

Energy supplied by ATP derived from cellular metabolism directly regulates cardiac function under aerobic conditions. The heart, like the brain, is an oxygen-consuming organ. Oxygen is consumed by the abundant mitochondria in the heart as ATP is produced through the respiratory chain reactions. An extremely large requirement for oxygen in the heart and brain indicate that these organs are also susceptible to ischemic insults; mitochondrial abnormalities may cause a brain-heart disease such as mitochondrial encephalo-myopathy. Basic and clinical researchers have extensively studied the pathophysiology of
USE OF MUTANT-SPECIFIC ION CHANNEL CHARACTERISTICS FOR RISK STRATIFICATION OF LONG QT SYNDROME PATIENTS

It was a great honor for me to receive the 2010 Richard J. Bing Young Investigator Award at the ISHR XXth World Congress in Kyoto, in my home country, Japan, for my work on correlation of electrophysiological and biophysical defects caused by Long QT syndrome type 1 (LQT1) mutations to the clinical phenotype in LQT1 patients.

After completion of my PhD at Jikei University School of Medicine (Tokyo, Japan), I was fortunate to join Prof. Arthur J. Moss’s and Dr Coeli MB Lopes’s group at the University of Rochester School of Medicine and Dentistry (Rochester, NY, USA) in 2008. Our group focuses on investigating the consequences of altering cardiac ion channel regulation for mutants linked to Long QT syndrome (LQTS) on cardiac risk and treatment effectiveness in patients. Prof. Moss has been involved in clinical and genetic research related to LQTS for over 20 years. He and his group have extensive experience in both clinical and statistical analysis of LQTS. Dr Lopes has over 15 years of experience in electrophysiology and using molecular biological techniques and heterologous expression systems to study cardiac ion channels. I am very excited to be part of this group and to employ this unique translational strategy for risk stratification and therapy management of LQTS patients.

ischemic heart disease; investigators have examined ischemia, hypoxia, ischemia-reperfusion, hibernation, ischemic injury, and ischemic preconditioning in the heart as well as in the brain.

Recent research interests have focused on the remodeling of the heart under pathological conditions since remodeling is directly related to the prognosis of patients with heart diseases. Ventricular hypertrophy and dilatation are the key processes of cardiac remodeling, and are often observed in patients with hypertension, ischemic heart disease and heart failure. Extensive studies have been performed to understand the structural and molecular basis of remodeling. Recent research on the molecular basis of cell death, i.e. necrosis, apoptosis and autophagy, also contributes to the understanding of the mechanisms of remodeling; however, the roles of fibroblasts and the extracellular matrix are not well understood. Vascular remodeling is also of keen interest as the phenotype of atherosclerosis. Recently, the role of the inflammatory response has been described, leading to a paradigm shift in our understanding of the pathogenesis of atherosclerosis and vascular injury.

In order to restore or prevent the pathological changes in the heart and vessels, many drugs have been developed (e.g. cardiotonic agents, α,β adrenergic receptor blockers, renin-angiotensin-aldosterone (RAS) inhibitors, statins, and anti-platelet drugs). In addition to these pharmacological treatments, repair with intrinsic cells, or ‘regenerative therapy’, is now being extensively studied, although the clinical benefits of this provocative approach have not been established.

Thus, understanding the unit of life is always the goal of research in the past, present and also in the future. An important issue in research is to recognize the researcher’s viewpoint – where are you standing on the plane of the unit of life? Many ISHR members stand on either the structure or metabolism axis. If so, it is important to pay attention to the other axes. A balanced view of all sides of the unit of life is critically important for scientists who study the biological activities of life.

Masatsugu Hori, M.D., Ph.D.
President ISHR
Can we use Genotype Information for the Risk Stratification of Long QT Syndrome?

Sudden cardiac death, due to fatal arrhythmias, is responsible for approximately 400,000 deaths annually in the US. The cardiac slow delayed rectifier K+ current (IKs) has been shown to underlie the development of cardiac arrhythmias. Mutations in the IKs α-subunit (pore subunit), KCNQ1, are linked to short QT syndrome, atrial fibrillation, and the most common form of inherited cardiac arrhythmia, LQT1. Current risk stratification of LQT1 includes mostly clinical risk parameters such as age, gender and the prolongation of QT interval (>500 ms QTc) observed in ECG, while mutation-specific risk stratification is rarely used to guide therapy for these patients, despite the increasing availability of genotyping. In this study, we investigated the association of biophysical ion channel functions (ion channel current magnitude, rate of current activation and deactivation, voltage dependence and maximal conductance) with the risk of cardiac events in LQT1 patients independent of traditional phenotypic risk factors such as QTc interval. We also further clarified the cellular mechanism underlying mutant-specific increase in cardiac risk by introducing an electrophysiology parameter into a transmural ECG computer model.

Slow Activated Kinetics of IKs Channel is the Novel Risk Factor for Cardiac Events in Long QT Syndrome Patients

The study population for this work was drawn from the International Long QT Registry (USA, The Netherlands, Japan, and Denmark). Clinical follow up data for patients enrolled over the past 20-30 years was used to compare cellular electrophysiology to cardiac risk. To allow better correlation of the mutant channel properties to the clinical course of patients carrying each mutation, mutations where clinical data was available for a large number of carriers were required. Thus, we only included mutations present in 10 patients or more. 387 LQT1 patients carrying 17 different missense mutations from the LQTS registry were used for this analysis (Fig. 1A). The electrophysiological parameters were obtained by two-electrode voltage clamp from expression of mutant ion channels in *Xenopus laevis* oocytes (Fig. 1B). Linear regression was used to test for correlation between ion channel characteristics and clinical phenotype and Cox proportional hazard regression was used to identify independent risk factors for cardiac events (syncope, aborted cardiac arrest, and sudden cardiac death). We found that slower rate of current activation significantly increased the risk of cardiac events (Hazard ratio: 2.02) independent of clinical parameters (gender, QTc and β-blocker treatment), whereas other ion channel characteristics did not independently affect the risk of cardiac events. Most interestingly, slow activation kinetics was still an independent predictor for cardiac events in patients with QTc <500 ms, while QTc did not predict cardiac risk (Hazard ratio: 2.10) (see also Fig. 2).

**Jin O-Uchi** (Rochester, NY, USA) was the winner of the 2010 Richard J. Bing Young Investigator Award at the XX ISHR World Congress (Kyoto, Japan; May 2010).
How does Slow Channel Activation Kinetics Increase the Probability of Cardiac Events in LQT Patients?

To study the mechanism underlying arrhythmogenesis of slow channel activation, we introduced the model IKs channels with slower activation kinetics into our original single cardiomyocyte model adapted from the Flaim-Giles-McCulloch (FGM) reconstruction of the canine cardiac cell. Slower channel activation rate caused the prolongation of APD duration in our model. We also developed a pseudo-transmural ECG model in which genetic mutations at the ionic channel level can be simulated and the resulting changes in the ECG can be assessed (collaboration with Dr John J Rice at IBM T. J. Watson Research Center, Yorktown Heights, NY). This ECG model predicted T-wave alternans due to early after depolarizations for mutations with slower activation rates (Fig. 3).

Conclusion

Our results suggest that slow channel activation impairs cardiac repolarization contributing to arrhythmogenesis in LQT1 patients. The results highlight the importance of genotype analysis for the risk stratification of LQT1 patients and its potential use for the mutant-specific therapeutic guidance in the future.

References


Jin O-Uchi, MD, PhD
Rochester, NY, USA
Dr Manabu Taneike

“Constitutive Autophagy is Necessary for Maintenance of Cardiac Structure and Function in Aged mouse Hearts”

Manabu Taneike¹, Osamu Yamaguchi¹, Issei Komuro¹, Noboru Mizushima² and Kinya Otsu¹.
Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Osaka¹; Department of Physiology and Cell Biology, Tokyo Medical and Dental University, Tokyo, Japan².

Dr Yin Liu

“Deficiency in Endothelial Nitric Oxide Synthase Impairs Fetal Coronary Artery Development in Mice”

Yin Liu, Xiangru Lu and Qingping Feng.
Department of Physiology and Pharmacology, Lawson Health Research Institute, University of Western Ontario, London, Ontario, Canada.

Dr Hisayuki Hashimoto

“Novel Method ‘Fucci’ Elucidated the Native Cell-Cycle Dynamics in Developing and Ischemic Cardiomyocytes”

Hisayuki Hashimoto¹, Shinsuke Yuasa¹, Shugo Tohyama¹, Tomohisa Seki¹, Toru Egashira¹, Yohei Ohno¹, Dai Kusumoto¹, Kojiro Yae², Masaki Kodaira¹, Hidenori Tabata³, Asako Sakaue⁴, Atsushi Miyawaki⁵, Keiichi Fukuda⁶.
Department of Cardiology, Keio University School of Medicine, Tokyo, Japan¹; Department of Regenerative Medicine and Advanced Cardiac Therapeutics, Keio University School of Medicine, Tokyo, Japan²; Department of Anatomy, Keio University School of Medicine, Tokyo, Japan³; Laboratory for Cell Function and Dynamics, Advanced Technology Development Group, Brain Science Inst, RIKEN, Saitama, Japan⁴.
Dr ROBBINS received his Ph.D. in Genetics and Development in 1976 from the University of Connecticut and, after taking a short fellowship with Jerry B. Lingrel, was appointed as Assistant Professor in the College of Medicine at the University of Missouri-Columbia. He rose through the academic ranks, and left Missouri to join the Department of Pharmacology and Cell Biophysics at the University of Cincinnati College of Medicine in 1987. In 1993 he moved to the Cincinnati Children’s Hospital to start the new division of Molecular Cardiovascular Biology and in July 2009, formed the Heart Institute, integrating the basic and clinical arms of Pediatric Cardiology. He currently is a Professor of Pediatrics, Chair, Division of Molecular Cardiovascular Biology, Associate Chair of the Research Foundation and Executive Co-Director of the Heart Institute. He has served on and chaired numerous national research review committees for the National Institutes of Health and the American Heart Association. He has served on 11 Editorial Boards, including the Journal of Molecular and Cellular Cardiology, is Associate Editor for a number of journals and has been Cardiovascular Section Editor for the Annual Review of Physiology for the past 9 years. He was recently named as a Senior Associate Editor for Circulation Research and, this past year, was chosen to Chair the National Study Panel for the American Heart Association’s program for establishing centers for Stem Cell Biology in the heart, the Jon DeHaan Competition.

Dr Robbins has been publishing in the field of cardiovascular biology for approximately 20 years. With over 180 publications during this period, his contributions have changed the way that basic cardiovascular research is done, by allowing the research community to carry out “gain-of-function” approaches specifically in the myocardium via cardiac-specific transgenesis. In a series of landmark papers, Robbins first defined the promoter elements needed to target and drive high levels of gene expression in the mammalian heart. Identifying the cis-trans interactions was what drove the basic research but, understanding the implications, Robbins then took the work further and explored the utility of cardiac-specific gene expression as a method of doing defined genetics in the mammalian four-chambered heart. After the initial proof-of-principal showing that cardiac specific transgenesis was feasible, he defined, built and tested a set of reagents that is now routinely used by hundreds of laboratories to carry out genetic experiments in the mouse cardiovascular system.

Dr Robbins unambiguously showed the utility of the general approach and developed a set of robust reagents that could be used by relatively inexperienced investigators to create animal models of cardiovascular disease. Dr Robbins’ work has changed the way in which we explore the basic pathology of cardiovascular disease. With well over 600 different models being developed and published using his reagents, the work that Dr Robbins published allowed the entire field to move forward at a pace undreamed of only 15 years ago. A contributing factor to the rapid spread of the technology was Dr Robbins’ early decision to make the reagents freely available, allowing the rapid dissemination of the needed tools, free from the confines of university intellectual property concerns.

Dr Robbins went on to use gain-of-function approaches to further his own investigations into the underlying pathologies of hypertrophic cardiomyopathy, as well as defining the structure-function relationships in a number of the contractile proteins.
His recent experiments have established the importance of mutations in the intermediate filament protein desmin and the chaperone, alpha B crystalline, as causative for a class of cardiomyopathies, which has recently led to the startling observation that intracellular pre-amyloids appear to play an important, and possibly generalized role in cardiovascular diseases of various etiologies.

In addition, recognizing the limits of the murine models for studying critical therapeutic avenues as well as certain aspects of human cardiovascular disease, Dr Robbins developed the ability to carry out cardiac specific transgenesis in the rabbit. This has already led to fundamental discoveries in hypertrophic cardiomyopathy, and allows the extension of cardiovascular gain-of-function to an animal whose cardiovascular system more closely resembles that of the human.

Dr Robbins’ recent work has focused on integrating the changes observed in contractile behavior with altered cardiomyocyte protein homeostasis and misfolding. Understanding the critical pathogenic pathways that link altered contractility with generalized deficits in protein folding may allow for the identification of novel therapeutic targets for the treatment of cardiovascular disease.
Jeffery D. Molkentin, Ph.D.

Thrombospondin4 is a Novel Regulator of ER Stress Adaptation and Cardioprotection

Winner of the 2010 Outstanding Investigator Award

(May 2010; Kyoto, Japan)

Dr. JEFFERY D. MOLKENTIN received his Ph.D. in physiology from the Medical College of Wisconsin in 1994, after which he completed postdoctoral training under Dr. Eric Olson at the University of Texas Southwest Medical Center in Dallas. In 1997, he joined Cincinnati Children’s Hospital Medical Center of the University of Cincinnati as a faculty member, where he rose through the academic ranks and was promoted to full professor before turning 40. He has won numerous awards, including selection as a Pew Scholar and the Katz Prize in cardiovascular research from the American Heart Association. Dr. Molkentin was an Established Investigator of the American Heart Association from 2003-2007 and is a full investigator of the Howard Hughes Medical Institute.

Dr. Molkentin serves as a full-time member of the National Institutes of Health (NIH) grant awarding study section CCHF (2006-2011), along with many other international review committees. He serves on a number of editorial boards, including The Journal of Biological Chemistry, The Journal of Clinical Investigation, Circulation Research and JMCC.

Dr. Molkentin has published over 245 original articles, including several landmark papers. His publications on calcineurin-NFAT signaling in the heart helped propel the field of signal transduction forward, and his original paper on the subject stands as the mostly highly cited research paper in Cell in 1998, with over 1,500 citations. His succeeding Science paper showed that calcineurin inhibition with cyclosporin A could prevent pathological cardiac growth in response to pressure overload, further defining the potential medical relevance of his initial discovery. His work in this area also spawned additional investigation into MAP kinase signaling and the calcium regulatory pathways that underlie pathological cardiac growth, two other areas where he is a leading figure.

Dr. Molkentin made major contributions to the understanding of regulatory proteins that control calcium-dependent cardiac contractility and hypertrophy. His 2004 Nature Medicine paper on PKCα defined a new calcium-dependent signaling paradigm that controls contractility at the level of the sarcoplasmic reticulum. This work was extended in a series of publications revealing a novel treatment for heart failure through PKCα inhibition.

More recently, Dr. Molkentin’s laboratory has taken a creative and leadership role in defining the relatively unexplored area of mitochondrial permeability transition pore functions as a key regulated step in the induction of cellular necrosis. His publication on cyclophilin-D null mice was one of the most highly cited papers in Nature in 2005. Understanding of the molecular mechanisms controlling cell death is of critical importance for virtually all types of human disease. For example, his laboratory showed that mitochondrial-regulated necrosis underlies muscular dystrophy in a 2008 Nature Medicine paper.

His work on cardiac signal transduction and the control of cell death by necrosis has established him as an international leader in cardiovascular sciences. Dr. Molkentin is widely respected for the depth, breadth and creativity of his work, as well as his collegiality and desire to foster the careers of young investigators.
THE KEITH REIMER DISTINGUISHED LECTURE 2010

PHENOTYPIC RESPONSES DUE TO INDUCED GENETIC ABLATION OF cMYBP-C IN ADULT MICE

HONORED SPEAKER: DR RICHARD L. MOSS

(MAY 2010; KYOTO, JAPAN)

Dr RICHARD MOSS is Director of the Cardiovascular Research Center and Senior Associate Dean for Research in the School of Medicine and Public Health at the University of Wisconsin. He received his Ph.D. in Physiology and Biophysics from the University of Vermont in 1975, followed by postdoctoral studies with Dr Fred Julian at the Boston Biomedical Research Institute. In 1979, Dr Moss was appointed Assistant Professor of Physiology at the University of Wisconsin, where he then served as Chair of Department from 1988 to 2009. During this time he led the founding of the Cardiovascular Research Center and the M.S. in Biotechnology degree program. Dr Moss was an AHA Established Investigator and currently holds an NHLBI Merit Award. He is the Robert Turell Professor of Physiology and recipient (2007) of an honorary Doctor of Medicine degree from Uppsala University.

Dr Moss presently serves on the editorial boards of Circulation Research, the Journal of Molecular and Cellular Cardiology, and the Journal of General Physiology. He is a Fellow of both the ISHR and the AHA. He has served as a member of the NIH Physiology Study Section (1993 to 1997), special emphasis panels at NIH, and several AHA review committees. Dr Moss was previously a member of the AHA Research Program and Evaluation Committee (1999-2003), the AHA Peer Review Committee (2002-2005), and the Executive Council of the Biophysical Society (1997-1999). He organized the 2002 Annual Meeting of the ISHR North American Section held in Madison, WI and has since served as President of the North American Section (2006-2009). Dr Moss is currently Past-President of the North American Section, has served on the ISHR-International Council since 2003, and was recently elected Secretary-General of ISHR-International.

Dr Moss’s research focuses on the roles of myofibrillar accessory and regulatory proteins as modulators of myocardial contraction in health and in diseases such as heart failure and heritable hypertrophic cardiomyopathies. He has co-authored more than 150 papers and has supervised more than 20 graduate students and postdoctoral fellows who now hold positions in academic medical centers and research institutions around the world. By biochemically extracting proteins from permeabilized myocardium, Dr Moss and his collaborators showed that thick filament proteins such as regulatory light chain and myosin binding protein C modulate the extent and rate of force development. Using knock-out, knock-in and transgenic approaches, they further showed that PKA phosphorylation of MyBP-C is principally responsible for the acceleration of myofibrillar contraction kinetics due to β-adrenergic stimulation. An emerging theme is that regulation of contraction via Ca²⁺ binding to troponin or the phosphorylation of accessory proteins such as MyBP-C involves modulation of positive cooperativity in the binding of cross-bridges to actin. Dr Moss’s recent work has focused on mechanisms of contractile dysfunction and Ca²⁺-triggered arrhythmias in hypertrophic cardiomyopathies due to mutations in MyBP-C.

IN MEMORIAM

DR RICHARD J. BING
1909 - 2010

We were saddened to hear of the passing of Dr Richard J. Bing, founder and first President of the ISHR, in La Canada, CA on November 8, 2010. A full obituary will be published in issue 18:3 of the newsletter.
JAMES DOWNEY received a BS degree from Manchester College in Indiana in 1967 and earned a PhD degree in Physiology at the University of Illinois in Champaign-Urbana in 1971 under the direction of Edward S. Kirk. Downey’s thesis research focused on factors affecting coronary blood flow. It was known that cardiac contraction compressed the coronary arteries with each beat throttling the blood flow to the heart muscle. Downey reasoned that if the mechanism of that interaction were understood then an intervention might be identified that could alter this interaction in a way that would increase perfusion of ischemic myocardium. That work resulted in Downey’s “waterfall” theory of the extravascular coronary resistance. Dr Kirk took a leave of absence from the University of Illinois halfway through Downey’s thesis research to do a sabbatical in Boston at Peter Bent Brigham Hospital, a Harvard teaching hospital. One of Dr Kirk’s former students Fred Downey (no relation) was a faculty member in the University of Illinois Veterinary school and generously invited James to finish his thesis experiments in his laboratory. Thanks to Fred Downey’s expert guidance the thesis was finished in a timely fashion.

Edward Kirk never returned to Illinois and instead became a staff member at the Peter Bent Brigham laboratory run by Edmund Sonnenblick. A very significant event in Downey’s stay in Boston occurred when Michael V. Cohen, then a young clinical fellow in cardiology with zero interest in research, was assigned a 6-month rotation in the “dog lab”. Against all odds, Cohen became hooked on basic research and that formed the basis of a life-long friendship and collaboration between the two scientists.

In 1979 Downey attended his first European meeting in Heidelberg, Germany. In a chance encounter he met Derek Yellon at one of the banquets and that was the beginning of another life-long friendship and collaboration. Yellon was then a junior staff member in David Hearse’s laboratory at St Thomas’ Hospital in London. Downey collaborated closely with Yellon and Hearse (also a former Peter Harris award recipient) over the next 7 years, exploring factors affecting...
myocardial infarction. Among other things, they developed several large and small animal models of infarct sizing that are still in wide use today. That transatlantic commuting ended in 1987 when both Downey and Yellon met their respective wives and could no longer justify being away from home for extended periods.

In 1991, Michael Cohen left his position in a New York hospital and joined the Division of Cardiology at the University of South Alabama. He and Downey have been collaborating closely ever since. That year they discovered that adenosine was the trigger for a highly protective, but little understood, phenomenon called ischemic preconditioning. They showed that the protection was due to signal transduction pathways and the bulk of their subsequent studies have concentrated on elucidating those pathways. Their discoveries include the role of: PKC, mitochondrial ATP-sensitive potassium channels as signal transduction elements, redox signaling, adenosine A₂b receptors, and PKG in preconditioning’s mechanism. Their studies of preconditioning’s signaling pathways has revealed many strategies for preconditioning a patient’s heart, some of which are now being evaluated in clinical trials.

Downey has published over 260 full papers. He sits on 4 editorial boards and has served on Circulation Research’s editorial board continuously since 1975. He has been active in the governance of the ISHR since the 1980s and served as President of ISHR-International from 2001 to 2004. Downey’s involvement with the ISHR brought him in contact with Peter Harris on many occasions to discuss society business. He has also been active in the governance committees of the American Physiological Society and the American Heart Association. In 2006 Downey was awarded a Doctor of Honoris Causa by the National and Kapodistrian University in Athens, Greece. Downey has mentored 5 PhD students and 26 post-doctoral trainees in his Alabama laboratory. Downey has always been a strong supporter of the ISHR’s mission of establishing international links among the world’s scientists. Accordingly, most of his students have come from abroad. Many were from Japan including Tetsuji Miura. Downey’s wife, Yukiko, is from Yamagata, Japan, and she always did her best to make the Japanese students feel at home in Alabama.

James M. Downey, Ph.D. is the ninth recipient of the Peter Harris Distinguished Scientist Award (Kyoto, Japan; 2010).

This Award of international importance is the highlight of each World Congress of the ISHR. It is conferred in recognition of lifetime achievements in the field of cardiovascular research.

Previous recipients are:

- Setsuro Ebashi, Japan (Melbourne, Australia; 1986)
- Albrecht Fleckenstein, Germany (Ann Arbor, USA; 1989)
- Robert B. Jennings, USA (Kobe, Japan; 1992)
- Howard E. Morgan, USA (Prague, Czech Republic; 1995)
- Lionel H. Opie, South Africa (Rhodes, Greece; 1998)
- Robert J. Lefkowitz, USA (Winnipeg, Canada; 2001)
- Arnold M. Katz, USA (Brisbane, Australia; 2004)
- David J. Hearse, UK (Bologna, Italy; 2007)
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