Dear Colleagues,

As we approach the congress kickoff and finish polishing the final details, we already have exciting news suggesting that this meeting will be a success. First of all, more than 250 abstracts were submitted in the initial call and we had the unprecedented number of 34 candidates for the Richard J Bing Young Investigators Award. Also, the congress program has settled into a provocative syncytium of 33 interconnected symposia with over 130 speakers that will cover all major themes of state-of-the-art cardiovascular research. Another highlight of the scientific program is the ISHR award lectures presented by: Dr. Heping (Peace) Cheng

El Puente de la Mujer (“Bridge of the Woman”) in Puerto Madero
2. Dr. Johannes Backs (Outstanding Investigator Award); Dr. Donald Bers (Peter Harris Distinguished Scientist Award); Dr. Rodolphe Fischmeister (Keith Reimer Distinguished Lecture); Dr. Edward Lakatta (Janice Pfeffer Distinguished Lecture) and Dr. Thomas Eschenhagen (President’s Distinguished Lecture). We are also greatly honored to have as the main attraction of our Congress the Nobel lecture delivered by Dr. Robert Lefkowitz (Chemistry Nobel Prize winner 2012).

Already more than 100 young investigators have signed in to attend the Early Career Investigators pre-congress event consisting of 2 symposia and a Career Development Panel discussion, which is the perfect start for our triennial reunion. For those who wish to discover a great city in addition to great science, you will find Buenos Aires to be a beautiful and eclectic city to explore. Just to give you a few facts about the city you will be visiting: After a frustrated first foundation in 1536, Buenos Aires was definitely founded in 1580 by Don Juan de Garay, a Spanish conqueror who led his old galleons towards the muddy coast of a brown river, the world’s widest river, “Río de la Plata”. The legend says that Don Juan decided to build the new city along the riverfront, close to where the presidential palace, “Casa Rosada” (pink house), is located today. One of many must-see spots, “Casa Rosada” is located in front of “Plaza de Mayo” (May Square) and the Buenos Aires Cathedral, where Archbishop Jorge Bergoglio, now Pope Francis, delivered mass until appointed Head of the Catholic Church. A few blocks south of May Square you can go relic hunting in the colonial neighborhood of San Telmo.

Walking west from May Square, on Avenida de Mayo, you can stop for coffee at the historic Café Tortoni and then keep walking up to the crossroad with 9

(schedule as of January 21, 2016)
de Julio Avenue, to get a glimpse of the “Obelisco”, another icon of this city. This monument is located at the crossroad of 9 de Julio and Corrientes Ave, the avenue that never sleeps! This area is famous for its theatres, pizza places and bookstores. A few blocks from there you will find the Colón Theater, the Opera House, which is a magnificent palace. If you want to go shopping, Buenos Aires offers a large number of luxurious shopping malls, such as Galerías Pacífico, at the end of Florida, the main pedestrian street in Buenos Aires.

As mentioned in the previous issue of this newsletter, the Congress venue, the UCA Convention Centre, is located in the district of Puerto Madero, a modern area of the city which harbours the latest architectural trends, the best restaurants, shops and bars of Buenos Aires and is only a few blocks away from the Ecological Reserve, a big green area, ideal for an afternoon stroll to enjoy local flora and wild life or to do bird watching in the very heart of the city!

Another important location to visit is the Recoleta cemetery, located in the ritzy Recoleta neighborhood, which is the resting place for many notable political figures and elites of Argentine history, including Evita Perón.

The chic, sprawling neighborhood of Palermo in north Buenos Aires is also a highly recommended destination. Palermo is known for its museums (Museum of Latin American Art of Buenos Aires; Malba, and the Museo de Bellas Artes or Fine Arts Museum), urban parks, like the Palermo woods with its rose garden walk (“Rosedal”), high-end boutiques, bustling cafés and bars, and cobblestone streets.

If you want to catch the spirit of the immigrant’s life at the turn of the 20th century and see the mythic birthplace of Tango, you must visit Caminito, in
the neighborhood of “La Boca”. And speaking of Tango, the musical hallmark of Buenos Aires, please remember that on April 21st we will close the Congress with an evening Gala Dinner and tango show at the historic Güemes Gallery. Don’t forget to reserve your tickets for this unique opportunity which will include transfer from the Convention Centre to Güemes Gallery, tango lessons, a 3 course meal with wine and an exclusive tango show featuring the music of Astor Piazzola, the pioneer of modern Tango. His work revolutionized traditional tango into a new style termed “nuevo tango”, which incorporates elements from jazz and classical music, and is exemplified by the well-known “Libertango”, performed by Grace Jones in Roman Polanski’s movie “Frantic”.

You are formally invited to combine the passion for unveiling the secrets of the heart with the fun of discovering Buenos Aires, a South-American pearl that deserves to be enjoyed – please register now if you have not yet done so!

For detailed congress information please visit our website at www.ishrbuenosaires2016.org.ar

We look forward to seeing you in Buenos Aires soon.

Professor Martin Vila Petroff, PhD
Chair XXII World Congress of the ISHR

Professor Alejandro Aiello, PhD
Co-Chair XXII World Congress of the ISHR

ISHR-European Section Winter Council Meeting in Paris

Members of the ISHR-ES Council in attendance at the Winter Council meeting in Paris, France (from left): Yoran Etzion, Alessandra Ghigo, Sandrine Lecour, Rodolphe Fischmeister (President-Elect), David Eisner (President), Lucie Carrier, Constantinos Pantos, Peter Ferdinandy (Past-President), Derek Hausenloy (Secretary) and Zoltan Papp.
Dear colleagues,

I have emphasized previously that the triennial World Congress is the ISHR’s premier event and principal USP. As the XXII ISHR World Congress in Buenos Aires and the contemporaneous end of my term as ISHR President draw ever closer, I thought this would be a good opportunity to review how the Congress has evolved over the period during which I have contributed to the management of the ISHR in an executive capacity.

I took office as ISHR Secretary General partway through the 2004 World Congress in Brisbane, Australia. Until that time, the organization and funding of the World Congress were largely the responsibility of the appointed local organizer(s), which predictably led to significant variations in both the scope and the balance sheet of the meetings. For reasons that I do not wish to review here, the Brisbane Congress required substantial additional support from ISHR International at a rather late stage, which together with the efforts of the leadership of the Australasian Section enabled a scientifically rewarding meeting to take place. That experience led to a review of the way in which the World Congress is organized and supported, such that through the ensuing 12 years and 4 meetings (Bologna 2007, Kyoto 2010, San Diego 2013 and Buenos Aires 2016) the Congress has become progressively more institutionalized and secure, while remaining representative of our members’ interests and retaining significant local historical and cultural flavour. The key contributions of ISHR International in the current World Congress model include the following:

• The Congress program, based on proposals from the global ISHR membership, is organized by a Scientific Program Committee (SPC) that is chaired by the Secretary General of ISHR International and includes subject experts from multiple ISHR Sections.
• The Secretary General is a de facto member of the Local Organizing Committee and acts as a liaison between this and the ISHR Executive Committee to focus and facilitate the practical aspects of planning the Congress, in particular the selection of venues and the agreement of contracts with local suppliers.
• ISHR International funds the core scientific program of the Congress, comprising 20-25 thematic symposia that are organized by the SPC.
• ISHR International funds 6 plenary lectures by award recipients, elected by the ISHR International Council.
• ISHR International helps secure and sponsor plenary lectures by Nobel Laureates, who have included Louis Ignarro (Bologna 2007), Oliver Smithies and Shinya Yamanaka (Kyoto 2010), Roger Tsien (San Diego 2013) and Robert Lefkowitz (Buenos Aires 2016).
• ISHR International funds the Richard J Bing Young Investigator Award, including travel awards for the selected finalists, and a Poster Award for each day of poster presentation.
• ISHR International sponsors dedicated Early Career Investigator activities, normally on the first day of the Congress.
• ISHR International, in liaison with ISHR Sections, provides Travel Awards for young investigators, to facilitate their attendance at the Congress.
• ISHR International hosts a dinner for Fellows of the ISHR (FISHR).

The intention of the ISHR International leadership is to maintain and further develop this model in the run up to the 2019 World Congress in Beijing and beyond. In that regard, during its meetings in Buenos Aires in April 2016, the ISHR International Council will receive and consider proposals from potential hosts of the 2022 World Congress. I look forward to reporting the outcome of those discussions in due course; in the meantime, I am confident (and relieved!) that I will step down as President with a structure firmly in place that secures the future viability and success of the ISHR World Congress.

I look forward to seeing many of you in Buenos Aires.

Metin Avkiran, PhD DSc
President, ISHR
The well documented finding that patients with ventricular premature systoles (VPBs) are at increased risk of lethal ventricular arrhythmias suggested that abolishing VPBs would prevent sudden cardiac death. However, several clinical trials have made it clear that drugs which reduce the frequency and complexity of VPBs can increase mortality.

**Ventricular Premature Systoles**

The electrocardiographic identification of VPBs in the early 20th century raised obvious questions regarding their clinical significance. Although VPBs are common and generally benign, they can be associated with a poor prognosis. In 1933, Lewis observed that patients with VPBs should have a high mortality because they are likely to have serious cardiac disease, so that although death might be triggered by VPBs it could also be caused by associated diseases (1). Lewis stated that evaluating the significance of VPBs would require comparison of two groups of patients, one with and one without VPBs, who were otherwise the same, and that “when such comparisons are made the significance of [VPBs will be] so slight that [their role] in determining the prospect of life becomes practically negligible.” (167).

It soon became clear that some VPBs are more dangerous than others. Commenting on their clinical significance, Louis Katz and Pick wrote in 1956: “premature systoles are frequently benign… Only when they are very frequent, occur in pairs or [triplets], and arise from multiple foci may the outlook be unfavorable for in these cases they are generally concomitant with organic heart disease.” (2163). Five years later a detailed “Lown Classification”, based on studies of patients following a myocardial infarction, graded VPBs in increasing order of severity: 0; none, 1; occasional, 2; frequent (>1/min or 30/ hr), 3; multiform, 4; repetitive (4a; couplets, 4b; salvos), and 5; early (“R on T”) (3). Although this classification came to be widely used, its predictive value was stated by the authors to be “preliminary” because it was based on “as yet inadequate data” (3135). The prognostic value of a simpler classification was documented by Ruberman et al. (4), who divided VPBs into two groups: Complex, which included (“R on T”), runs of two or more, multiform (two or more morphologies), and bigeminoal (normal - VPB - normal - VPB etc.); and simple, where the VPBs had none of these features. All-cause and sudden death mortality were subsequently shown to be more than twice as high in patients with complex VPBs than those with simple VPBs, while the latter differed little from those with no VPBs (5). However, not all VPBs are caused by the same mechanism, for example VPBs during the acute phase of a myocardial infarction have different underlying mechanisms than those which appear later (6), and so can require different treatment.

**Antiarrhythmic Drugs**

Recognition of their adverse effects on prognosis led to efforts to abolish VPBs using drugs that had been used to treat atrial arrhythmias. The latter have a long history. In 1749 Sénac observed that Cinchona tree bark could terminate “rebellious palpitations” (7); this symptom, now known to be caused by atrial fibrillation (AF), was a common complication of the then prevalent rheumatic heart disease.

*In Memoriam*

Dr Arnold M Katz
1932-2016

Regrettably, this will be the final article in the Truth from Error series, as we were saddened to learn of the passing of Dr Arnold M Katz (Professor of Medicine Emeritus, University of Connecticut School of Medicine, and Honorary Professor of Medicine and Physiology, Geisel Medical School at Dartmouth) on January 25, 2016. A full obituary will be published in issue 22.3 of the newsletter.
Sénac’s observation attracted little notice until 1923 when Wenckebach described a merchant who had frequent attacks of an irregular rhythm that, although they caused little disability, led him to seek medical help because he would like to have “good order” in his heart as well as in his business (8). When Wenckebach admitted he could not promise effective treatment, the merchant asked why there were heart specialists “if they could not abolish this very disagreeable phenomenon”, and stated that he knew how to abolish the arrhythmia. That night the merchant took a gram of “quinin” prepared from cinchona bark, which according to Wenckebach was “a sort of drug for everything” (8472), and returned the next day with a regular pulse. Quinidine, the most effective cinchona alkaloid, soon became standard treatment for treating AF.

Sixty years ago life-threatening AF was treated by giving large doses of quinidine every few hours until either sinus rhythm was restored or the patient’s heart stopped; the latter made it clear that antiarrhythmic drugs could have dangerous “proarrhythmic” effects. Happily this risk can now avoided by electrical cardioversion.

Prevention of Sudden Cardiac Death

The increasing occurrence of acute myocardial infarction in the 1960s led to the development of coronary care units and cardioversion that made it possible to identify and treat patients at risk for sudden cardiac death. At the same time, new drugs that reduced the frequency and complexity of VPBs became available. This led to clinical trials designed to show that treating VPBs increased survival. Unwisely I initially made fun of these trials, suggesting that like shooting fish in a barrel a positive result was foreordained. How wrong I was. One after another, clinical trials showed that antiarrhythmic drugs could increase mortality, often causing the trials to be stopped. Drugs found to shorten survival include the sodium channel blockers mexilitine (9), encainide and flecaïnide (10), moricizine (11) and lidocaine (12); the potassium channel blocker d-sotalol (13); and calcium channel blockers (14).

Proarrhythmic Effects

Drugs that reduce the frequency and complexity of VPBs may increase sudden death mortality because the mechanisms which cause ventricular fibrillation can differ from those that increase the number and complexity of VPBs. This interpretation is supported by the findings that a re-entrant mechanism called a “rotor”, which depends in part on the onward rectifier current i_K1, can cause ventricular fibrillation (15); and that quinidine and chloroquine, which have similar effects on many of the membrane currents that participate in VPBs, differ in their effects on these rotors (16). Another explanation for the adverse effects of some antiarrhythmic drugs is their ability to depress conduction, which is proarrhythmic as well as antiarrhythmic. This can be understood by comparing this situation to walking through a snake pit when a sleeping viper awakens; the “antiarrhythmic” effect of shooting the drowsy viper (the VPB) can be overwhelmed by the “proarrhythmic” effect of startling dozens of previously dormant snakes (ventricular fibrillation) (17). It is clear, therefore, that much remains to be learned about the anti- and proarrhythmic effects of existing drugs and potential new approaches to medical therapy.

Some “Practical” Considerations

Calculations of the “practical” value of research such as that described in this article can provide valuable insights. The Woman’s Health Initiative Trial, a large randomized trial simulated by basic research, cost ~$260 million but yielded the counterintuitive result that reducing the use of supplemental hormones in postmenopausal women improved, rather than worsened, survival (18). Analysis of this trial showed that between 2003 to 2012 decreased hormone use reduced the number of patients receiving this therapy by ~4.3 million; decreased breast cancer cases by ~126,000 and cardiovascular disease by ~76,000, and yielded an economic return of ~$37.1 billion (~$140 for each dollar spent in the trial) (18). Although the costs and value of the research described in the present article have not been calculated, the findings described above helped stimulate the development of implantable electronic defibrillators to replace antiarrhythmic drugs.

continued on page 14
**Report on the XXXII Japanese Section Meeting:**

**Cardiovascular and Metabolic Week 2015**

*(December 10-12, 2015; Kobe, JAPAN)*

This year’s Annual Scientific Meeting of the ISHR-Japanese Section was organized by Prof. Yoshihiko Saito from Nara Medical University and was held in Kobe – one of Japan’s big port cities – famous for delicious Wagyu meat (the celebrated “Kobe Beef”) and a winter light festival called “Luminarie” that is held every December to commemorate the Great Hanshin-Awaji earthquake of 1995.

The special feature of this year’s annual meeting was the collaboration with three other scientific meetings; the 23rd annual meeting of the Japanese Vascular Biology and Medicine Organization, organized by Prof. Toyoaki Murohara from Nagoya University, the 19th annual scientific meeting of the Society of Cardiovascular Endocrinology and Metabolism, organized by Prof. Kazuo Kitamura from Miyazaki University, and the 37th annual meeting of the Cardiac Biopsy Conference, organized by Prof. Hiroyuki Tsutsui from Hokkaido University. These four meetings were held jointly from December 10 to 12 in the same venue, Kobe International Conference Center, and the joint meeting was christened Cardiovascular and Metabolic Week 2015 (CVMW2015). Each society pursued its own field of interest, while at the same time expecting that the collaboration would stimulate new ideas by way of a scientific “chemical reaction”. Throughout this joint meeting, the participants explored scientific fields outside of their own specialties and the interaction between participants resulted in new insights. A total of 704 meeting delegates participated in many enthusiastic discussions.

The meeting started with a joint special lecture by Prof. Ryozo Nagai (Jichi Medical University) on important factors and systems in cardiovascular study. He lectured on the importance of both elementary study at the cell and molecular level, showing how the character of vascular cells changes under various stresses, and systemic study, clarifying the interactions between different cells, tissues and organs. In another joint special lecture, Prof. Kenneth Walsh (Boston University) spoke about the mechanistic links between metabolic dysfunction and cardiovascular disease. He presented the mechanisms by which obesity contributes to adipose tissue dysfunction and discussed how this dysfunction leads to systemic changes that affect the way cardiovascular tissues respond to stress.

The 3rd joint special lecture was presented by Prof. Junichi Sadoshima (New Jersey Medical School), who discussed the effects of the Hippo pathway on the regulation of cardiomyocyte fate. He demonstrated the role of the Hippo pathway in cardiomyocyte hypertrophy, proliferation and regeneration using loss of function and gain of function mice models.

The 4th joint special lecture was presented by Prof. John C. Burnett, Jr. (Mayo Clinic) on the roles of natriuretic peptides in cardiovascular disease. His laboratory has engineered designer natriuretic peptides which have more beneficial properties than endogenous natriuretic peptides, and he presented a highly innovative strategy in peptide therapeutics.
In addition to these 4 joint special lectures, CVMW had 4 joint symposia, 9 luncheon seminars, 5 evening seminars and a four presidents’ lecture session. All of these joint sessions were very well-attended and the research presented gave the participants much food for thought.

ISHR had its own sessions; an award lecture, two symposia, three oral sessions, 9 poster sessions and a YIA session. Prof. Kinya Otsu (King’s College London) was awarded The 2015 Janice Pfeffer Distinguished Lecture for his work entitled “Mitochondrial quality control, sterile inflammation and heart failure”. He lectured on the importance of understanding the molecular mechanisms underlying the axis of hemodynamic stress, mitochondrial damage, mitochondrial dynamics, mitophagy and inflammation to develop novel therapeutics against heart failure.

The themes of the ISHR symposia were “Molecular mechanisms of cell differentiation and morphogenesis during cardiovascular development”, and “Molecular mechanism for heart failure”. In these sessions, a total of 9 presenters gave excellent talks. Active and fruitful discussions were stimulated by the 18 presentations in the three oral sessions, and the 49 presentations in the seven poster sessions.

In the Young Investigators Award session, 6 finalists out of 19 applicants presented their data. All presentations were well organized and very interesting. Dr. Ayako Seno (Nara Medical University) won the first prize of the session for her work on the cardio-renal syndrome.

At the end of the second day of the meeting, a wonderful reception was held in the banquet hall of Kobe Animal Kingdom, a theme park of animals and flowers. After an alpaca welcomed the participants, they celebrated the success of the joint meeting and deepened relationships with each other.

The 32nd ISHR-Japanese section annual meeting, held jointly with 3 other scientific societies, was quite successful with no less than 700 participants. We believe this collaborative style of scientific meeting generates novel ideas drawn from the diverse participants, which will advance study in each field. We thank all of the participants who supported this meeting and look forward to the 33rd annual ISHR-Japanese Section meeting in 2016 organized by Prof. Keiko Takihara from Osaka University.

Kenji Onoue
Yoshihiko Saito
First Department of Medicine, Nara Medical University

Dr. Kenneth Walsh gave a wonderful presentation on the mechanistic links between metabolic dysfunction and cardiovascular disease.

Dr. John C. Burnett, Jr. gave a special lecture on the role of natriuretic peptides in cardiovascular disease.

ISHR reception at a wonderful banquet venue under many plants and flowers. Dr. Keiko Takihara informed participants about the next ISHR Japanese section meeting.
Report on the XXXIII European Section Meeting
(July 2-5, 2015; Bordeaux, France)

The 33rd ISHR European Section (ISHR-ES) Annual Meeting was a special one for the European Section as it was the first “back to the traditions” stand-alone ISHR-ES meeting since the 32nd meeting that took place in Haifa, Israel in 2011. In 2012 in London, ISHR-ES was one of the organizer sister societies of the Frontiers of Cardiovascular Biology (FCVB) meeting organized by the Council of Basic Sciences of the European Society for Cardiology. In 2013 the World ISHR meeting took place in San Diego, CA, USA so no ISHR-ES meeting was organized. Then in 2014, ISHR-ES held a one day focused meeting that continued with a collaborative meeting with FCVB in Barcelona, Spain. In 2015, in order to preserve the identity of ISHR-ES and to maintain the traditional family-like atmosphere of the meeting, the 33rd ISHR European Section Annual Meeting was held in the beautiful French city of Bordeaux. The Bordeaux meeting was also special because the ISHR International Council decided to support regional meetings by organizing the international council meetings during regional ISHR meetings. Therefore, the Bordeaux meeting was heavily supported by the presence of International Council members and their colleagues which significantly contributed to the scientific excellence and the great overall success of the meeting. The almost 500 participants made this meeting the largest ISHR-ES meeting in the last 20 years and ensured ample attendance at all sessions. In spite of the extremely hot days throughout Europe during the meeting, speakers and the audience coped with temperatures over 40 degrees centigrade and filled up even the plenary sessions organized in an almost open-air lecture hall. The main social event, as one may guess in the “world capital of wine”, was a wine tasting dinner at the beautiful Château Giscours.

In addition to 27 scientific sessions, the plenary sessions of ISHR award lectures and ceremonies were real celebrations of science. The “Outstanding Investigator Award” lecture was delivered by Thomas Thum (Mh-Hannover, Germany). The “Peter Harris Distinguished Scientist Award” lecture was shared jointly this year by Drs Roberto Bolli (Univ of Louisville, USA) and Jon Lederer (Univ of Maryland, USA). The “Distinguished Leader Award” was presented to David Hearse, London, UK after a laudation given by Metin Avkiran, President of ISHR-International. The “President’s Distinguished Lecture” was delivered by Ruiping Xiao (Beijing Medical Univ, China).

The “Medal of Merit” award of ISHR-ES was delivered to Fabio Di Lisa, former ISHR-Intl Treasurer, Asa Gustafsson, presents the 2015 ISHR Outstanding Investigator Award to Thomas Thum after his lecture.

The 2015 ISHR-ES/SERVIER Research Fellowship was awarded to Pietro Ameri by Sophi Nisse-Durgeat, Director of CV Scientific Communication, Servier International.

ISHR-Intl Past-President, Masatsugu Hori (left), and ISHR-ES Past-President, Peter Ferdinandy (right), present the 2015 ISHR Peter Harris Distinguished Scientist Award to Roberto Bolli.

ISHR-Intl President, Metin Avkiran (left), and ISHR-Intl Secretary-General, Richard Moss (right), present the 2016 ISHR Distinguished Leader Award to David Hearse, former President of ISHR-Intl.
president of ISHR-ES after a laudatio
given by Peter Ferdinandy, Past-President
of ISHR-ES. The 2015 ISHR-ES/Servier
Research Fellowship was awarded to
Pietro Ameri (Univ of Genova, Italy)
who briefly summarized his proposal
entitled “Modulation of the NOTCH sig-
naling pathway of ER=rbB2: role in the
cardiotoxicity of ErbB2 – targeted ther-
apy”. The 2014 winner, Alicia D’Souza
(Univ of Manchester, UK) gave a sum-
mary of the work she had carried out on
“Targeting microRNA to reverse exercise
training-induced bradyarythmias”. Both
presentations convinced the audience that
the ISHR-ES/Servier research fellowships
had been awarded to excellent candidates.

ISHR-ES gratefully acknowledges the
impeccable organization of the 2015
meeting by the local organizers, Pierre
Dos Santos and Rodolphe Fischmeister,
President-Elect of ISHR-ES.

Peter Ferdinandy,
Past-President, ISHR-ES

Please visit http://ishr2015.u-bordeaux.fr/
en/Presentation/Photo-album/r522.html
to view a photo album of the Bordeaux
meeting.
Dr. Åsa B. Gustafsson received her Ph.D. in Bio-medical Sciences in 2001 from the University of California San Diego (UCSD). She completed her postdoctoral training at the Scripps Research Institute (TSRI) in La Jolla and in 2005, joined the faculty at TSRI. She left TSRI to join the Bioscience Center at San Diego State University in 2007. In 2009, she was recruited to the Skaggs School of Pharmacy at Pharmaceutical Sciences at UCSD where she is currently an Associate Professor of Pharmacy and Pharmacology. Dr. Gustafsson won the ISHR North American Section’s Young Investigator Award in 2005 and the Western Pharmacological Society’s Keith and Eva Killam Memorial Award in 2010. She was awarded the AHA Established Investigator Award in 2014. She is also a Fellow of the American Heart Association (AHA).

Dr. Gustafsson also serves on a number of grant review panels for the National Institutes of Health (NIH) and AHA. She is currently is a full-time member of the MIM NIH study section (2012-2018). She is a member of several editorial boards, including Circulation Research, American Journal of Physiology-Heart & Circulatory Physiology and Journal of Molecular and Cellular Cardiology.

Dr. Gustafsson has made several major scientific discoveries that have significantly contributed to the advancement of cardiovascular science. She currently leads a growing research program at UCSD in the areas of mitochondrial function and autophagy. Dr. Gustafsson’s research is focused on understanding the molecular pathways that regulate the life and death of cardiac myocytes. Mitochondrial dysfunction and activation of cell death pathways are common occurrences in cardiovascular disease and contribute to the development of heart failure.

More recently, her research has focused on pathways and proteins that regulate clearance of mitochondria via autophagy (mitophagy) in the heart. She is investigating how the BCL-2 proteins and the PINK1/Parkin pathway recognize and mark dysfunctional mitochondria for degradation via the autophagy-lysosomal pathway. Among her many key scientific contributions in this area was a publication describing how myocardial ischemia/reperfusion injury leads to removal of damaged mitochondria via the autophagy-lysosomal pathway. This finding was important because it identified autophagy as a protective response activated by myocytes to prevent unnecessary cell death. She also discovered that the induction of mitophagy during I/R is mediated by the pro-apoptotic BH3-only protein Bnip3. In subsequent studies, she discovered that Bnip3 is a potent inducer of mitophagy and that this function is separate from its role as a pro-death protein. She also discovered that Bnip3 functions as an autophagy receptor on the mitochondria to tether the mitochondria to the autophagosomes.

Her studies on Bnip3 and mitochondrial autophagy led to the discovery that Bnip3 induces translocation of the E3 ubiquitin ligase Parkin to mitochondria. She was the first to demonstrate that Parkin plays a critical role in clearing dysfunctional mitochondria in response to stress such as a myocardial infarction and that defects in Parkin-mediated mitophagy lead to the rapid development of heart failure. Most recently, she uncovered that MCL-1, an anti-apoptotic BCL-2 protein, is essential for mitochondrial homeostasis and induction of autophagy in the heart. She discovered that in addition to its anti-apoptotic function, MCL-1 is also a critical regulator of mitochondrial function and autophagy. These findings have important clinical implications; for example, MCL-1 is highly expressed in cancers and many biopharmaceutical companies are developing therapeutic drugs to inhibit MCL-1.

Dr. Gustafsson’s research on mitochondria and autophagy in the myocardium has provided new important insights into how mitochondrial turnover via autophagy is regulated in the myocardium. Overall, her successful track record as a scientific investigator and laboratory head has established her as a leader in cardiovascular sciences.
Evangelista Kranias, Ph.D.

Calcium Circuits in the Heart: a Matter of Life or Death

Winner of the 2014 Peter Harris Research Achievement Award

(May 12-15, 2014; Miami, Florida)

Dr. Evangelia (Litsa) G. Kranias is currently a Distinguished University Research Professor, Hanna Professor of Cardiology and Director of Cardiovascular Biology in the Department of Pharmacology & Cell Biophysics at the University of Cincinnati College of Medicine. She is also the co-Director of the Cardiovascular Center of Excellence. She received her BS degree from the University of Chicago (1970) and her Masters and Ph.D. degrees under L. R. Dumas from Northwestern University, Chicago (1974). She served as a postdoctoral fellow under R. A. Jungmann at Northwestern University Medical School, Chicago (1974-77). In 1978, she started her faculty career at the University of Cincinnati Medical Center, where she became a full professor in the Department of Pharmacology & Cell Biophysics in 1988.

Dr. Kranias’ internationally recognized research program has provided fundamental insights into the regulatory mechanisms and signaling pathways underlying calcium homeostasis in cardiac physiology and pathophysiology with special emphasis in heart failure. Dr. Kranias has also extended her basic research findings to the clinical arena and has elucidated the functional significance of Ca-handling in the deteriorated function of human failing hearts. She was the first to identify human mutations in calcium cycling genes and show that these may predispose to arrhythmias and heart failure. The overall goal of Dr. Kranias’ research program is to build a comprehensive understanding on the role of calcium cycling in cardiac contractility and cell survival.

Early in her scientific career, Dr. Kranias recognized the importance of a small molecule, phospholamban (PLN), in the regulation of calcium cycling through the sarcoplasmic reticulum and the overall regulation of cardiac function. Her biochemical work showed that phospholamban regulates specific steps in the calcium ATPase enzymatic process, implicating this molecule as a regulator of cardiac function. Subsequently, Litsa Kranias with John Solaro were the first to demonstrate (Nature: 1982) that phospholamban is phosphorylated in the heart on a beat-to-beat basis. This was the first evidence of the physiological importance of this protein and its significance in “flight-or-fight” situations.

In parallel studies, the Kranias lab pioneered studies on isolation and characterization of the sarcoplasmic reticulum protein kinases and phosphatases that regulate calcium transport and thus, cardiac relaxation. This provided evidence of a multimeric compartmentalized complex, which reversibly regulates calcium cycling in the cardiomyocyte.

Dr. Kranias’ in vitro, biochemical studies were then extended to in vivo settings and she provided the first evidence that controlling the levels of phospholamban alone, it is possible to fine-tune the heart’s pumping action. Dr. Kranias has also extended her basic research findings to the clinical arena and showed that the phospholamban levels are relatively higher in individuals with heart failure, which may contribute to the impaired calcium handling and cardiac function. This led the Kranias lab to a search for human phospholamban mutations that may be associated with heart failure. The first two mutations in the human phospholamban gene were identified in 2003 and both appeared to be deleterious in the human population. This was the first indication that genetic alterations in human calcium cycling genes are also associated with dilated cardiomyopathy.

Over the last decade, Dr. Kranias continued to identify novel regulators of calcium cycling and cell death. One of them is HAX-1, the anti-apoptotic protein, which interacts with PLN and serves as an additional regulator of sarcoplasmic reticulum calcium cycling and apoptosis. The other one is the small heat shock protein 20 (Hsp20), which along...
with inhibitor-1 attenuates the phospho-lamban phosphatase activity and protects the heart from apoptosis and remodeling under stress conditions. In addition, the intraluminal histidine-rich Ca-binding protein (HRC) was found to interact with the calcium-ATPase (SERCA) and regulate the enzyme’s maximal Ca-transport velocity. Recent studies indicate that this multimeric SERCA/PLN-ensemble is involved in heart failure and arrhythmias, as well as apoptosis and cell death. Dr. Kranias has also identified human variants in these calcium-cycling genes that affect their “activity”, reflecting aberrant Ca-handling and increased cell death.

Dr. Kranias’ research has been funded by the National Institutes of Health (NIH) for the past 3 decades, often with multiple awards. She received both a NIH Research Career Development Award (RCDA) and a Method of Extension in Time (MERIT) Award. Her scientific investigations have been published in over 225 original manuscripts and 75 invited reviews. Dr. Kranias has been invited to organize, chair and speak at numerous National and International scientific meetings. She has also been a dedicated mentor for young scientists: she has graduated 22 Ph.D. students and mentored 47 post-doctoral fellows/research associates. Dr. Kranias has received many National and International awards and honors. These include the Daniel Drake Medal, which is the highest honor of the UC Medical Center, the American Heart Association Samuel Kaplan award, the Janice Pfeffer award from the ISHR and an Honorary Doctorate degree from the University of Athens. In 2009, Dr. Kranias was named an AHA Distinguished Scientist and in 2012, she was elected as a corresponding member of the Academy of Athens. Dr. Kranias served on the National Council of the Biophysical Society, the National Council of the ISHR (International and NA-section) and the AHA Research Committee. She has also served as Associate Editor or an Editorial Board member of several journals and a member of numerous review committees.

In 2014, this award combined the Research Achievement Award and the Peter Harris Distinguished Scientist Award given in previous years.

References
1. Lewis T. Diseases of the Heart. New York; Macmillan. 1933
17. Katz AM. Physiology of the Heart 5th Ed. Philadelphia; Lippincott/Williams and Wilkins. 2011 p. 485, Fig. 16-62.
ECI Symposiums – Research presentations by ECIs

- Monday, April 18, Symposium A: 8:30; Symposium B: 10:20 in the Aula Magna (UCA 1st floor)
- Presentations were chosen in a competitive process from submitted abstracts.
- Coffee and informal discussion will be available between symposium A and B and before the Panel Discussion.

ECI Panel Discussion – “Publishing: A Career Development Panel”

- Monday, April 18, 12:10 in the Aula Magna (UCA 1st floor)
- A panel of editors and associate editors from some of the most prestigious journals in cardiac research will give advice and answer questions about the ins and outs of publishing for early career scientists.

ECI Lunch with members of the ISHR-International Council – meet the ISHR leadership!

- Monday, April 18, 13:00 in the foyer of Juan Pablo II (UCA 2nd floor)
- A pizza and empanada buffet lunch will be complimentary for those who sign up during registration.

ECI Social – Network with your fellow ECIs!

- Tuesday, April 19, 20:00 at the Barbaroja Bar (an artisanal beer bar)
- The Barbaroja is located off-campus (a pleasant 15 min walk from the UCA).
- Your $10 Ticket (available through the Congress registration site) entitles you to 2 half pints (or 2 soft drinks) and light hors d’oeuvres (additional drinks and food can be purchased).

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