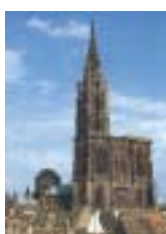




THE NEWS BULLETIN OF THE INTERNATIONAL SOCIETY
FOR HEART RESEARCH



**STRASBOURG,
FRANCE**

JUNE 21-24, 2003

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**MYSTIC,
CN, USA**

**JUNE 28 -
JULY 1, 2003**

12 13

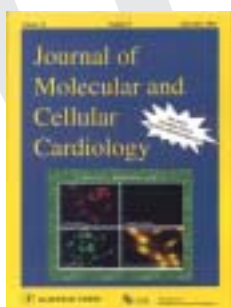


**BRISBANE,
AUSTRALIA
AUGUST 7 -11,
2004; XVIII
ISHR WORLD
CONGRESS**

8 14

IN THIS ISSUE:

2001 Peter Harris Award 1
 Past Truth & Present Poetry 3
 President's Letter 5
 Medal of Merit of European
 Section 6
 2001 Research Achievement
 Award 7
 2004 World Congress in
 Brisbane 8
 2002 Outstanding Investigator
 Prize 10
 Report on Strasbourg Meeting 11
 Report on Mystic Meeting 12
 2003 Janice Pfeffer Lecture 13
 Call for Nominations for the
 2004 Richard Bing, Peter
 Harris and Research
 Achievement Awards 14
 Meetings Calendar 15



<http://jmcc.editorialmanager.com>
for online submission
of manuscripts

ROBERT J. LEFKOWITZ

**WINNER OF THE SIXTH
PETER HARRIS
DISTINGUISHED
SCIENTIST AWARD**



ROBERT J. LEFKOWITZ was born in the Bronx, New York City in 1943. The only child of Max and Rose Lefkowitz, he had set his sights on the goal of becoming a practicing physician as early as elementary school. Highly focused on this goal, he graduated from Columbia College with a Bachelor of Arts Degree at age 19 and from Columbia University College of Physicians and Surgeons at age 23. After an internship and one year of medical residency at Columbia Presbyterian Medical Center, he moved in 1968 to the NIH to fulfill his two-year military obligation as a Clinical and Research Associate at the National Institute of Arthritis and Metabolic Diseases (NIAMD, as it was then called). During the subsequent two years, he worked together with Jesse Roth and Ira Pastan and developed the first radioligand binding assay for ACTH receptors leading to his very first publication in *The Proceedings of the National Academy of Sciences*. This study was amongst the first to label a membrane receptor with a radioligand and was contemporaneous with the early work on the nicotinic cholinergic receptor. This first research experience greatly excited him, but he moved to Boston to finish his clinical training in General Internal Medicine and Cardiovascular Diseases at the Massachusetts General Hospital. During this period (1970-73)

(continued on page 2)

he began working in the laboratory of the Chief of Cardiology, Dr Edgar Haber, a noted immuno-chemist, and initiated the studies that ultimately formed the basis for his life's work on adrenergic receptors. In July of 1973, he moved to Duke University as an Associate Professor of Medicine and Biochemistry and started his own independent research program. In 1976, he became an Investigator of the Howard Hughes Medical Institute, a position he holds to this day. He became a James B. Duke Professor of Medicine and Biochemistry in 1982.

Working with the adrenergic receptors as models, Dr Lefkowitz's research has formed the basis for the now vast field of research into so-called G protein-coupled or seven membrane spanning receptors. This, the largest superfamily of membrane receptors, includes approximately one thousand members in the mammalian genome and regulates virtually all physiological processes from hormonal and neurotransmitter signaling to sensory signaling in the visual, olfactory and taste systems to chemokine signaling. Virtually all cardiovascular regulation is controlled by members of the seven membrane spanning receptor superfamily such as the adrenergic and muscarinic cholinergic receptors, angiotensin and endothelin receptors and many others.

In the early 1970's, Lefkowitz and his numerous students and fellows systematically developed ligand binding approaches for the study of each of the then-known adrenergic receptors, both $\alpha 1$ and 2 and $\beta 1$ and 2. They then developed methods to solubilize, photoaffinity label and ultimately purify by affinity chromatography each of these receptors. In the 1980's, they were able to obtain small amounts of protein sequence from the purified receptors and clone their genes and cDNAs. This cloning, together with collaborators at

Merck, of the gene for the $\beta 2$ -adrenergic receptor, announced in *Nature* in 1986, revealed its homology and secondary structure relationship to the visual pigment, rhodopsin. The common theme of seven membrane spanning domain receptors was rapidly confirmed in work by his laboratory on the other members of the adrenergic receptor family. This early work made possible the cloning of essentially all the other members of the vast superfamily of receptors by various homology techniques over the ensuing fifteen years.

Lefkowitz also unraveled the molecular mechanisms underlying the phenomenon of desensitization of receptors, in the process discovering and cloning the G protein-coupled receptor kinase and β -arrestin families of proteins which regulate this universally important regulatory phenomenon. More recently, he has found that G protein-coupled receptor kinases and β -arrestins not only desensitize receptors, but can link them to novel signaling pathways. Exciting new functions for the arrestins are being reported by laboratories around the world including their important role in mediating clathrin-mediated endocytosis of the receptors.

His laboratory has also made numerous other discoveries about the molecular mechanisms of functioning of the receptors, how they signal, interact with G proteins, *etc.* They also discovered the phenomenon of constitutively active mutant receptors, now known to be the cause of an ever-growing list of human diseases.

Now 60 years old, he continues as actively engaged in his research as ever, with the major current focus being on unraveling the novel signaling roles of β -arrestins and G protein-coupled receptor kinases. His approaches range over the entire spectrum from genetically altered knockout and transgenic animals

to detailed molecular and structural studies. Despite all of his accomplishments in research, the professional accomplishment of which he is most proud is the training of a large number of extremely successful and productive investigators. Almost 200 individuals have worked in his laboratory over the past 30 years, many of whom have gone on to distinguished careers as scientists and administrators in both the academic and commercial settings.

For his research, Lefkowitz has received dozens of awards. He is a member of the USA National Academy of Sciences, the Institute of Medicine and the American Academy of Arts and Sciences.

Dr Robert J. Lefkowitz is the sixth recipient of the Peter Harris Distinguished Scientist Award (Winnipeg, Canada; July 2001).

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:

- Dr S. Ebashi (Melbourne, Australia; 1986)
 - Dr A. Fleckenstein (Ann Arbor, USA; 1989)
 - Dr R.B. Jennings (Kobe, Japan; 1992)
- [HEART NEWS AND VIEWS 1993; 1(2): 1-3]
- Dr H.E. Morgan (Prague, Czech Republic; 1995)
- [HEART NEWS AND VIEWS 1995; 3(3): 1-5]
- Dr L.H. Opie (Rhodes, Greece; 1998)
- [HEART NEWS AND VIEWS 1999; 7(3): 3-6 and 2000; 8(1): 4-5]

Past Truth & Present Poetry

TALES FROM THE PAST, when told to a new generation, create little interest, particularly when they recount personal events only. However, when they deal with flesh and blood men and women and of the eddies in the stream of time, they hold our attention. A look in the past can reveal the origin of ideas and relate them to the men and women who create them. This tale is an attempt to recount developments in medical science as personally experienced during the last seventy years. I hope this will show that science is a child of its time bound to thoughts and technology of its time. Therefore, we should not apply today's standards to the work that came before us.

In 1935, a year after I had obtained my M.D. degree, I was a research fellow at the Carlsberg Biological Institute in Copenhagen, Denmark, which was financed by the Carlsberg Brewery. The institute was built primarily for the study of cell cultures. The director of the Institute was Albert Fischer, a student of Alexis Carrel from the Rockefeller Institute, now the Rockefeller University in New York City. What was tissue culture like in the early part of the 20th century? I had been exposed to this technique in the early 1930s as a medical student in Berlin, volunteering for Rhoda Erdman, a pioneer in the field of tissue cultures. In 1907 Ross Granville Harrison, when at Johns Hopkins Hospital, was the first to devise a method to grow tissue fragments outside the body. He not only initiated this technique, but also was able to show that nerve fibers develop from particular nerve cells in the brain and the spinal cord. Harrison placed the tissue derived from a frog on a cover slip, inverted it over a hollow ground microscope slide and sealed it with paraffin. When Harrison was

23. AN ODYSSEY IN SCIENCE AND MEDICINE



Richard J. Bing

proposed for the Nobel Prize for a second time, the committee eliminated him because "of the rather limited value of the method and the age of the discovery." In my early Hopkins days in 1943 my laboratory at Johns Hopkins Hospital was close to that of George Otto Gey who, using his roller tube technique, propagated cells, viruses and malignant cells in vitro for long periods of time. Gey is remembered particularly for his growth of malignant He-La cells in cell cultures. The word He-La is an abbreviation of the name of a young woman with cervical cancer whose tissue was cultured. Gey was a tall outgoing man who always welcomed young investigators to his lab. Harrison's experiments attracted the attention of Alexis Carrel. In 1909 Carrel sent his assistant Montrose T. Burrows to Harrison to learn the method and adapt them to the tissues of warm-blooded animals. Carrel introduced sterile technique and the Carrel flask, which could accommodate more tissue and medium. This led to the development of synthetic and defined media. In 1913 Conti in France introduced the time-lapse camera which showed migrating and dividing cells. Today's tissue culture

has become an essential tool in the growth of viruses, of cancer cells and the study of biology of tissue.

In 1937 I received a Rockefeller fellowship to work at the Rockefeller Institute in New York with Alexis Carrel. Carrel was born in France and received the Nobel Prize for his work on organ transplantation; he also contributed to the development of cell culture. He was an unusual scientist who believed in parapsychology; but he was an inspired innovator, a scintillating personality whose interests in non-scientific matters did not endear him to the staff at the Rockefeller Institute. He made the vital mistake of returning to France when the Nazis occupied it, in the vain hope of helping his beleaguered country. To me, Carrel was a great teacher and a friend. Among the scientists at the Rockefeller Institute were Oswald Avery, Peyton Rous and Karl Landsteiner. I had the opportunity to talk to members of their department, the contact facilitated by a faculty dining room, presided over by a painting of Lavoisier and his young wife. Landsteiner had received the Nobel Prize for his discovery of blood groups. He was one of those scientists who liked to work at the bench, trusting only results which he himself had personally obtained. A simple experimental arrangement led to his discovery of blood groups. As he wrote in his Nobel lecture from 1930, "my experiments consisted of causing the blood serum and erythrocytes of different human subjects to react with one another." He concluded that "it became clear that the reactions follow a pattern which is valid for the blood of all humans, and that the peculiarities discovered are just as characteristic of the individual as are the serological features peculiar to an animal species.

Basically, in fact, there are four different types of human blood, the so-called blood groups. The number of the groups follows from the fact that the erythrocytes evidently contain substances with two different structures, of which both may be absent, or one or both present in the erythrocytes of a person.” His discovery made the use of blood transfusions possible.

Another Nobel Prize winner at the Institute was Peyton Rous. I found him always willing to talk about his work. He had been for many years the editor of the *Journal of Experimental Medicine*, and was a strict judge. He even edited the famous paper by Avery on the transformation of pneumococci, but it is questionable whether this great contribution needed his editorial work. He received the Nobel Prize in 1966, when he was over eighty for the discovery of a virus which produces tumor in chickens. Rous in 1910 “described a malignant chicken sarcoma which could be propagated by transplanting its cells, these multiplying in their new hosts and forming new tumors of the same sort.” He mentioned that “its cells yielded a causative virus.” It is now recognized that cancer is the result of many genetic mutations and dysregulations of cellular pathways which lead to the formation of new blood vessels through angiogenesis. In solid tumors, the cells form a wide variety of signaling systems which include angiogenic factors. Viruses are just some of the myriad of factors which can lead to dysregulation. The search goes on!

The third in this constellation at the Rockefeller Institute was Oswald Avery. He never did receive the Nobel Prize, although he richly deserved it. A Canadian by birth, he received his MD from the College of Physicians and Surgeons of Columbia University. He became interested in the factor which transforms rough into smooth pneumo-

cocci; Avery demonstrated that DNA and not proteins is responsible for the transformation into the genetic machinery of the rough cells.

After a surgical internship at the College of Physicians and Surgeons of Columbia University under A. O. Whipple, the initiator of the Whipple procedure for carcinoma of the pancreas, I joined the department of physiology at New York University under Homer W. Smith whose scientific interest was renal physiology. Smith was also a great writer, a novelist who had the gift to express his ideas on evolution with originality and style. In renal physiology Smith used the concept of clearance introduced by Rehberg and van Slyke. Biochemistry had not made inroads into renal physiology. At Bellevue Homer W. Smith was the center of the group working on the role of the kidney in hypertension and shock, and Dickinson Richards and André Cournand began their work on catheterization of the heart, primarily interested in pulmonary circulation. Cournand was a careful and systematic worker, while Richards was interested in the grand design. He was a humanitarian and a scholar, a highly cultured New Englander and an all-round scholar. Cardiology at that time was primarily concerned with flow and pressure and right heart catheterization was an ideal tool to study these new parameters.

During World War II I spent time in the medical corps and the chemical warfare division of the US Army. I later joined the department of Surgery at Johns Hopkins Hospital under Alfred Blalock, to work on congenital heart disease. It was an exciting time. Cardiac surgery was in its early stages and Blalock had just published his early results on the surgery of congenital heart disease. This gave us the opportunity to define, by means of right heart

catheterization and other physiological tests, the circulatory changes in these disorders. Open-heart surgery was still in the future; therefore Blalock’s technique was limited to conditions that could be treated by methods that avoided direct surgery on the heart itself. The work on congenital heart disease was carried out with a group of brilliant young surgeons.

At that time, we noticed that catheterization of the coronary sinus in man could be carried out at will. From then on our work was primarily concerned with the extraction and utilization of foodstuffs by the human heart and their contribution to its oxidative metabolism. We continued this work at the University of Alabama in Birmingham and found that the heart was, as Taegtmeier expressed it, “an organ with metabolic flexibility.” It uses carbohydrates, fats and amino acids according to their availability, and myocardial failure is not accompanied by changes in myocardial extraction of foodstuffs. We began to recognize that the heart is a metabolic organ rather than a mere pump, which regulates and is regulated by flow and pressure. Alabama was followed by Washington University in St. Louis, by Wayne State University in Detroit, and finally by the Huntington Medical Research Institute in Pasadena. In Detroit we introduced coincidence counting in the determination of human coronary flow *in situ*.

I hope this incomplete tale has brought out some general facts about the progress of clinical and fundamental research. Yesterday’s research looks primitive and simple as compared to the present. But I would venture that our successors 50 years from now will look at today’s research with the same degree of condescension that we reserve for the work of our predecessors. Science and art are the children of the times during which they are created. The style

PRESIDENT'S LETTER



THE MEETINGS SEASON

SUMMERTIME is the season for warm breezes, green trees and of course ISHR meetings. I was able to attend the European Section meeting in Strasbourg, France and the American Section meeting in Mystic, Connecticut. The South American Section met in August in Buenos Aires as did the Australasian Section in Melbourne. The latter two of course are technically winter meetings in the southern hemisphere but who is going to quibble. The only non-summer meetings seem to be the Japanese Section meeting in late November and the Indian Section meeting which is traditionally held mid-winter to avoid the fierce summer heat in India. I will be attending the Tokyo meeting in November. The meetings are doing well despite the rather austere economic climate at present. The Strasbourg meeting was an experiment in which the ISHR combined forces with the European Society of Cardiology to have a joint meeting. There were mixed reviews about the combined format. Clearly the ESC staff outnumbers the ISHR staff and they had the conference site well decorated with ESC banners such that the ESC had a much higher profile than the ISHR. Also the ESC registration was considerably larger than the ISHR but that was in part due to many delegates having dual membership. Those with dual membership were apparently registered as ESC. That issue aside, the program was well planned and the talks were excellent. Gerd Heusch from Essen, Germany gave the second annual Keith Reimer Lecture, and Ketty Schwartz and Jutta Schaper received special awards for their exemplary service to science and the ISHR. The venue could not have been better. The old city center was charming with the ancient single-spired cathedral and the picturesque Alsatian buildings each leaning at a slightly different angle. My wife accompanied me and she thoroughly enjoyed it. Kudos goes to Jean-Jacques Mercadier for organizing a superb meeting

Mystic was equally as nice. The weather was totally cooperative. This bucolic seaport was also an ideal venue. There were museums, a great aquarium and even a casino if you were financially adventurous. The highlight of the meeting for me was to spend some time with our past JMCC editor Arnold Katz. Arnold who had been suffering from a serious illness now has recovered and participated in the meeting with as much vigor as ever. He gave a spectacular after dinner talk at the banquet. Piero Anversa from New York Medical College gave the first annual Janice Pfeffer memorial lecture. Again the science was first class and Dipak Das and Bruce Liang are to be congratulated for their outstanding efforts.

(continued on page 6)

of creation changes, but human nature changes little. There also should be close dialogue between research carried out at the bench and at the bedside. Research should, like Claude Lenfant expressed it, "gather from the tree of knowledge fruit for the solace and refreshment of mankind."

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Richard J. Bing, M.D.

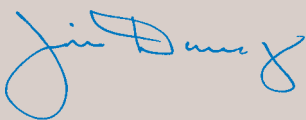
(continued from page 5)

ISHR AWARDS AND THE PRESIDENT'S PAGE

On another front, we have created yet another avenue for communication between the ISHR and our membership. We now will publish the President's Page in the *Journal of Molecular and Cellular Cardiology*. This will be published on an *ad hoc* basis whenever we have something to communicate quickly to the membership. Be sure to check every issue of the JMCC to see if it has a President's Page and if so, read it to get the latest news from the ISHR. The first President's Page will serve to solicit applications or nominations for the society awards that will be presented at Brisbane next year. The first award is the Richard Bing Young Investigator Award. Investigators who will be under 36 years old at the Brisbane meeting will be eligible to apply. The second award is the Research Achievement Award. This goes to the most outstanding investigator under the age of 55 at the time of the congress. Persons competing for this award must be nominated by a colleague as self-nominations are not allowed. Eduardo Marbán won this award at the last World Congress in Winnipeg. The final award is the Peter Harris Distinguished Scientist Award which goes to the individual who has displayed a lifetime of outstanding research achievements. Robert Lefkowitz received the Peter Harris award in Winnipeg. There is no age limit. Again, the candidates must be nominated by a third party. Details of how to apply or nominate a candidate for the above awards can be found on the ISHR web site www.ishrworld.org.

BRISBANE WORLD CONGRESS

Lindsay Brown continues to circle the globe touting the virtues of the upcoming World Congress in Brisbane. I believe he has hit every Section Meeting this year and he must have really racked up some impressive frequent flyer mileage. Just beware of deep vein thrombosis, Lindsay. The program is progressing nicely and we will co-meet with the pharmacology society who's meeting will use the same venue and immediately precede our meeting. I have looked at airfares to Brisbane and, while the airlines are not giving them away, they were not awful either. They are only slightly more than Europe for us in the US. There are also some great satellite meetings being offered. I have elected to go to the ischemia meeting in the Kruger national park in South Africa. Angina is often described by patients as an elephant sitting on your chest. Maybe I will find out what that really feels like. There are also great meetings in Iguazu Falls (Argentina), Hong Kong and Melbourne (Australia). See the ISHR web site for contact details and schedules.



James M. Downey

MEDAL OF MERIT OF EUROPEAN SECTION

During the European Section Meeting in Strasbourg (June 2003), the Medal of Merit was awarded for the first time. This Medal is given in recognition of scientific achievements and in gratitude for service to the European Section of the ISHR. The first recipients of the Medal of Merit were Jutta Schaper (Germany) and Ketty Schwartz (France). In 1981, Jutta (left on the picture) was elected Secretary General of the European Section, a position which essentially combined those of Secretary and Chairman. In 1992, she was succeeded by Ketty, who held the position of Secretary General until 1998.



**EDUARDO MARBAN, M.D., PH.D.
WINNER OF THE FIRST RESEARCH
ACHIEVEMENT AWARD
(JULY 2001; WINNIPEG, MANITOBA)**

**CELLULAR BIOLOGY OF ISCHEMIC
PRECONDITIONING**

EDUARDO MARBAN, a native of Havana, Cuba, came to this country with his parents at the age of six as a political refugee. He earned his B.S. in mathematics from Wilkes College in Pennsylvania, and then attended the Yale University School of Medicine in a combined M.D./Ph.D. program. (M.D. 1980, Ph.D. in Physiology one year later). Dr Marbán was an intern and medical resident on the Osler service at the Johns Hopkins Hospital. During his internship and residency, he held a secondary appointment as a research associate in the Department of Physiology at the University of Maryland. The following year he became a fellow in the division of cardiology at Johns Hopkins under Myron Weisfeldt.

Appointed to the Johns Hopkins University faculty as an assistant professor in the Department of Medicine in 1985, Dr Marbán was promoted to associate professor of medicine in 1988 and in 1991 achieved the rank of full professor. In 1992, he was appointed director of molecular and cellular cardiology at Johns Hopkins. In 1998, Dr Marbán became director of the newly-established Johns Hopkins Institute of Molecular Cardiobiology, an inter-departmental program designed to foster fundamental research into the workings of the heart.

In 1999, Dr Marbán was honored as the first faculty member, to be named to the Michel Mirowski, M.D. Professorship in Cardiology. This endowed professorship was dedicated in honor

of Dr Mirowski, the inventor of the automatic implantable defibrillator. In 2003, Dr Marbán became the Chief of Cardiology at Johns Hopkins; he also inaugurated the Donald W. Reynolds Cardiovascular Clinical Research Center at Johns Hopkins, a \$24 million 4-year program focused on identifying novel risk factors for sudden cardiac death.

During his extraordinary career, punctuated by frequent triumphs such as the Basic Research Prize of the American Heart Association (AHA), the Lucian Award, the Distinguished Service Award of the Council on Basic Cardiovascular Sciences (BCVS) of the AHA, a SCOR award and a Center on Proteomics Award from the NIH, and the recent Reynolds Center Award of the AHA, Dr Marbán has redefined the meaning of success. With astonishing rapidity, he has risen to leadership positions in virtually all activities in which he has involved himself, as exemplified by his appointment as Chair of the CVA Study Section of the NIH, Chair of the Council on BCVS of the AHA, Chief of Cardiology at Hopkins, Editor of *Circulation Research*, and Director of the Reynold Center.

Despite these multifarious responsibilities, he has continued to publish not only copiously, but also in the most stringent journals. Dr Marbán has made fundamental contributions in several areas, including excitation-contraction coupling, the disorders of ionic homeostasis that underlie ventricular arrhythmias, and the molecular basis of



myocardial ischemia/reperfusion injury. In a series of classic studies, he showed that myocardial “stunning” in rodents is caused by loss of contractile protein sensitivity to activator calcium, secondary to modifications induced by reactive oxygen species. Recently, he has elucidated a critical role of KATP mitochondrial channels in preconditioning and their response to adenosine and nitric oxide.

Dr Marbán has trained dozens of cardiovascular scientists, many of whom have gone on to successful careers, and has built a formidable research team that is at the leading edge in cardiovascular medicine worldwide. At the young age of 49, Dr Marbán is already a legend.

The purpose of this Award is to recognize an outstanding scientist who has made major and independent contributions to the advancement of cardiovascular science and who is likely to further develop his/her research in the future. The Award is bestowed triennially at ISHR World Congresses and is sponsored by Chugai Pharmaceutical Company.

The first Award was given to Dr Eduardo Marbán, during the XVII World Congress in Winnipeg, Manitoba.

BRISBANE

XVIII WORLD CONGRESS INTERNATIONAL SOCIETY FOR HEART RESEARCH AND THE 52ND ANNUAL SCIENTIFIC MEETING OF THE CARDIAC SOCIETY OF AUSTRALIA & NEW ZEALAND

CARDIOLOGY BENCH TO BEDSIDE: THE SCIENCE AND THE PRACTICE
7-11 AUGUST 2004

BRISBANE CONVENTION & EXHIBITION CENTRE BRISBANE QUEENSLAND AUSTRALIA

NOW that all the members of the ISHR know that the World Congress will be held in Brisbane next August, it is time to make the decision on which one or more satellites you want to attend! This is your opportunity to participate in some superb scientific sessions in fantastic locations - and it will break up the long trip to Australia, or a great way to start the journey for the Latin American members. For most people, the travel costs will be similar since a round-the-world ticket usually costs only slightly more than a return flight from Europe or North America to Australia. And, as you are members of the only worldwide organization devoted to cardiovascular research, each satellite will be held on a different continent!

THE FIRST pre-congress satellite to consider is *Heart failure 2004: an integrated basic and clinical approach*, held from August 1-3 at the magnificent Iguazu Falls on the border of Argentina and Brazil in South America (see also <http://www.austral.addr.com/iguazu/morep>). This satellite will also serve as the XIII meeting of the Latin American section of the ISHR. The organizing committee, Alicia Mattiazzi and Martín Vila-Petroff, have proposed an excellent series of plenary sessions, symposia, interactive sessions with students and researchers as well as poster sessions. Symposia include EC Coupling and Myofilament

Proteins - Contribution to Heart Failure; The NHE in Cardiac Hypertrophy; Repair of the Failing Myocardium; The Ischaemic Heart; and Therapeutic Strategies in Heart Failure. This satellite will allow the interaction of basic and clinical researchers, interns and trainees, as well as clinicians and cardiologists to discuss the only major cardiovascular disease that is increasing in incidence - heart failure. For details, contact Martín Vila-Petroff - Centro de Investigaciones Cardiovasculares - Facultad de Ciencias Médicas 60 y 120 (1900), La Plata - Argentina - Tel/Fax: +54 221 4 834833; E-mail: mvila@atlas.med.unlp.edu.ar.

The conference dates have been chosen so that participants can then fly with Lan Chile to Santiago. The trip continues with QANTAS (the conference airline) on QF322 leaving Santiago at 23.25 on August 4th and arriving in Sydney at 7.25 on August 6th (remember you cross the International Dateline). That day, QANTAS will be operating at least 16 flights for the one-hour connecting flight to Brisbane.

THE NEXT pre-world congress meeting will be convened by Salvatore Pepe from August 3-5 at the Baker Heart Research Institute in Melbourne, Australia. This satellite will consider another critical issue in current cardiovascular research: *Ageing heart and vessels: current understanding,*

new research and the challenge of reducing the health care impact of age-related cardiovascular disease.

The multi-disciplinary program will consist of 10 symposium sessions plus a moderated poster session, over two and a half days. The topics will range from basic to clinical science within themes such as: Myocardial Structure & Function; Vascular Ageing; Ageing in Health vs Disease; Age-Related Response to Injury & Stress; Thrombosis & Fibrinolysis; Risk Factors, Comorbidity & Therapeutic Strategies; Quality of Life Care; Novel Therapies; and Clinical Trials.

Melbourne is a major international entry point into Australia and offers a vast choice for the visitor, including the arts, entertainment, cuisine, and fashion. Melbourne is a gateway to the best grape growing and wine-making districts in Australia but also to wild and unique national parks that includes breathtaking coasts and forested mountains. In addition to social events, the conference will also offer registrants a half day mid-meeting break with organised tour options to the Yarra Valley and Mornington Peninsula wine districts, Dandenong Mountain Ranges for walking, native flora & fauna, Healesville Wildlife Sanctuary, or tours of the city and bay. For details, contact Salvatore Pepe (spepe@baker.edu.au; Tel. +61385321310; Fax +61385321314),

or visit www.baker.edu.au/ishr. QANTAS have direct flights from Melbourne to Brisbane every hour on Friday, August 6th, 2004, from 6.05 until 21.05; the trip takes about 2:20 hours.

Now - how can you take in more science on the way home from the Brisbane meeting? Join a post-congress satellite in either the Kruger National Park in South Africa, or in Hong Kong!

THE KRUGER SATELLITE will emphasise *Cellular injury in ischaemia* from August 13-15, 2004. With your "round the world" tickets from the OneWorld group (see more details at <http://www.oneworldalliance.com/>), be sure to book yourself on Flight QF501 or 503 on Thursday, 12th August 2004, immediately after the Conference, from Brisbane to Sydney. You will then be in time to catch Flight QF63 to Johannesburg at 10.00 arriving that same evening at 16.10. Our local travel agent, Nicky Krugel, will arrange accommodation in Johannesburg on Thursday night, and then for your transport to the Kruger Park on Friday. You will find the travel agent's contact details at <http://ishr.sun.ac.za>, which also contains details about the Satellite Meeting, with links to information on the Kruger Park.

Lionel Opie will deliver the Opening Address at the Friday evening welcoming party. Other prominent speakers include Jim Downey, Gary Lopaschuk, Roberta Gottlieb and Gerd Heusch. In addition to a full scientific programme, there will be ample opportunity for delegates and accompanying persons to explore the magnificent setting of the meeting, by going on game rides through the Park, and relaxing in the African bushveld. The rest camp, Berg-en-Dal, is situated in the most picturesque, and game-rich part of the Kruger Park.

The venue is a virtual "island" setting, which means that all the accommodation,

subsistence, and social event costs for delegates and accompanying persons are covered by a single all-inclusive fee. The registration fee is the only additional cost for delegates. Persons wishing to stay on in the Kruger Park after the Meeting, or those who would like to make use of the occasion to see more of South Africa, are encouraged to contact the local travel agent. Late

August is a very good time of the year to visit Southern Africa.

Keep watching the satellite homepages as well as www.heart2004.com for all updates! So - how many continents will you be visiting for the next World Congress of the ISHR?

(continued on page 15)



Iguazu Falls on the border of Argentina and Brazil. Site of the South American pre-world congress satellite.

KEY DATES

Early registration and abstract deadlines:

Brisbane World Congress:
All Satellites:

February 29, 2004
March 31, 2004

**PETER CARMELIET, M.D., PH.D.
WINNER OF THE FIRST
OUTSTANDING INVESTIGATOR PRIZE
(JULY 2002; SZEGED, HUNGARY)**



PETER CARMELIET was born on December 8, 1959. He is married and has three children. Dr Carmeliet graduated from the University of Leuven, Belgium, as M.D. in 1984 and Ph.D. in 1989. He performed a post-doctoral training in molecular neurobiology at Harvard Medical School (1989-90) and in functional genomics at the Whitehead Institute, M.I.T., Cambridge, MA with Dr Mulligan (1990-91). He was promoted to the rank of Associate Professor in 1994 and of Full Professor of Medicine at the University Leuven in 2000. In 1995, he became vice-director of the Center of Transgene Technology and Gene Therapy, Leuven. Dr Carmeliet has been appointed Visiting Professor of Medicine at the University of Brussels (1995-97), Professor of Medicine at CARIM, University of Maastricht, Netherlands (2000-now), and Visiting Professor at the University of Darmouth, New Hampshire, US (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 became acquainted with the recently developed techniques of generating mice with (conditional) inactivation or mutation of target genes, adenoviral gene transfer and transplantation of bone marrow cells. Using these novel gene-technologies, Dr Carmeliet generated 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 have led to novel insights in the role of plasminogen in angiogenesis and various cardiovascular

disorders including hemostasis, atherosclerosis, restenosis, aneurysm formation, pulmonary and systemic hypertension, cardiomyopathy, *etc.*

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 expression of VEGF is regulated by hypoxia via hypoxia-inducible factors (HIFs). Meticulous phenotypic analysis of additional gene-targeted mice have led to unpredicted findings. For instance, loss of HIF-2 α and inhibition of VEGF impair lung maturation *in utero*, while treatment with VEGF prevents fatal respiratory distress in premature mice. Dr Carmeliet 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 in the enigmatic pathogenesis and raises hope for treatment of this fatal disorder. Outside of the angiogenesis field, Dr Carmeliet developed transgenic mice models for long QT3 cardiac arrhythmia, endochondral bone formation and Zellweger syndrome.

The scientific research of Dr Carmeliet, translating genetic and molecular insights into novel therapeutic opportunities, has been published in *Nature* (6), *Nature Med* (13), *Nature Genet* (4), *Cell* (1), *J Clin Invest* (14), *PNAS* (7), *Circ Res* (3), *Circulation* (6), *J Biol Chem* (4), *Cardiovasc Res* (4), *Annals NY Acad Sci* (4), *etc.* He is the recipient of honorary memberships and several awards and has served on Advisory Boards of the Max Planck Institute, the Wellcome Trust, Cancer Research Institute Lausanne, International Cancer Research Treatment Torino and on Editorial Boards of several prestigious journals. Since 1994, more than 30 pre- and postdoctoral students from Europe, USA, Canada and Japan have been trained in his research group.

The purpose of this Prize is to recognize an outstanding scientist who has made major and independent contributions to the advancement of cardiovascular science and who is likely to further develop his/her research in the future. While the Research Achievement Award is presented during the ISHR World Congress, the Outstanding Investigator Prize is given at Section Meetings.

The first Prize was given to Dr Peter Carmeliet, during the XXII European Section Meeting in Szeged, Hungary.

JOINT MEETING IN STRASBOURG REPORT ON THE XXIII EUROPEAN SECTION MEETING, TOGETHER WITH THE ESC WG ON HEART FAILURE (JUNE 21-24, 2003; STRASBOURG, FRANCE)

This year the charming city of Strasbourg accommodated the annual meeting of the European Section of the ISHR. Breaking with tradition, the scientific efforts of the European Section were joined with those of the Working Group on Heart Failure of the European Society of Cardiology. The end of June was a perfect timing since exceptionally warm, sunny weather welcomed the participants. The congress was held in a spacious, well air conditioned conference centre situated next to the buildings of the European Parliament.

One of the goals of this joint meeting was to bring basic scientists and clinicians closer together. The conference started with eight basic science symposia, covering topics such as stem cells and a genomic approach for the treatment of pathological conditions. These innovative approaches were discussed again later in an integrated clinical - basic science session *How to mend a broken heart* that was chaired by Drs Dreyfus and Cohen-Solal. Speakers included Drs Schwartz and Menasche. The Keith Reimer Distinguished Lecture on Coronary microembolization was delivered by Dr Gerd Heusch from Essen,

The biography of Dr Gerd Heusch will appear in the next issue of HEARTNEWS AND VIEWS.

Germany. The first day was concluded with the opening ceremony and a cocktail reception in the exhibition halls.

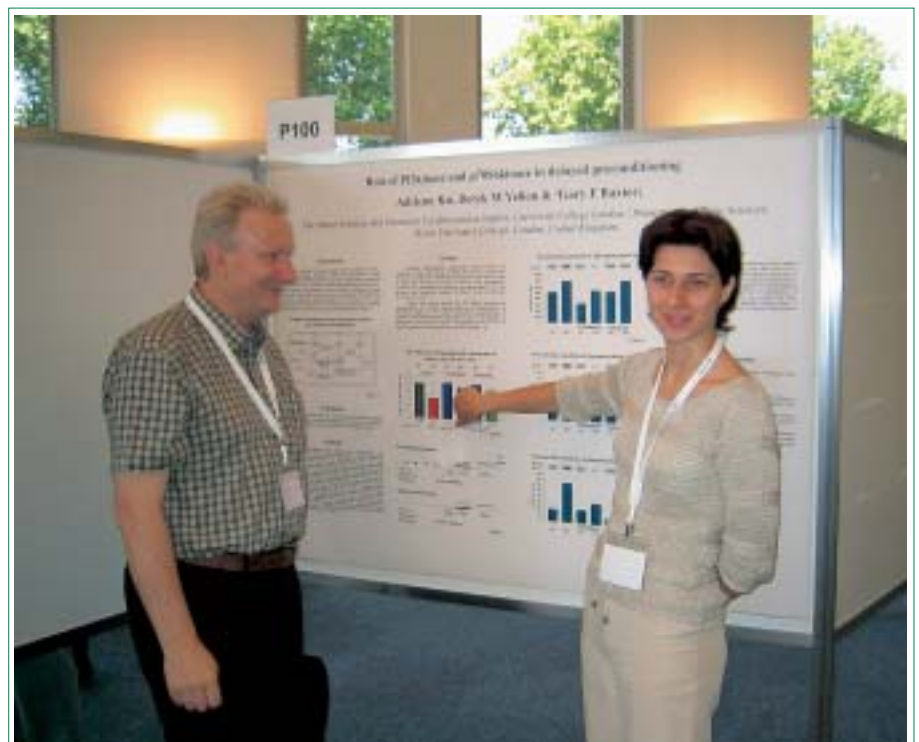
In the session *Late braking trials*, the results of clinical trials such as COMET and COMPANION were presented. While we were slipping from one hall into another one, there was ample opportunity to visit the area where

hundreds of posters were presented, with two days of moderated poster sessions. The morning after the gala dinner in the charming *Ancienne Douane*, where we could meet our old friends, was dominated by basic and clinical Young Investigator Award competitions. Dr Grieve (London, UK)

was the winner of the basic science competition and was awarded by the ISHR for his study 'Pivotal role of NADPH oxidase in cardiac contractile dysfunction and fibrosis induced by chronic pressure-overload'.

Strasbourg offered many possibilities to relax, enjoy the sunshine on one of the terraces near the beautiful cathedral or have dinner in a restaurant in the *Petite France* area. Although the clinicians outnumbered the basic scientists, this joint meeting was a successful attempt to integrate basic and clinical science. We are grateful to Dr Jean-Jacques Mercadier, Past-President of the European Section and Co-Chairman of the Scientific Committee for organizing a meeting that was scientifically excellent and socially very enjoyable. See you next year in Dresden!

Adrienn Kis, Ph.D.
London, UK



Dr Kis is discussing her poster 'Role of PI3 kinase and p70S6 kinase activation in delayed preconditioning' with Dr Barton from Harefield, UK.

JUICY MYSTIC PIZZA REPORT ON THE XXVTH AMERICAN SECTION MEETING

(JUNE 28-30, 2003; MYSTIC, CONNECTICUT)

The XXVth North American Section Meeting was held at the Mystic Hilton, Mystic, Connecticut from June 28th to 30th 2003. Mystic is a small town famous for its seaport. In this meeting, many investigators gathered and discussed science together from breakfast to the evening ceremonies. In the forum session of the first day, it was shown that alcohol, especially wine, has a beneficial role in reducing the risk of cardiovascular disease. This forum seemed to encourage some investigators to consume alcohol in the evening reception. Known by all movie aficionados, Mystic has some famous pizza stores and "Mystic Pizza" is a hit movie about three young women who lived here and worked at a pizza store.

If this scientific meeting could be compared to a "Mystic Pizza", I would consider the setting where the meeting was held as the *crust*. Mystic has a very comfortable atmosphere that seemed to encourage the attendees to actively discuss scientific matters during each session. The special keynote address by Prof. Roberto Bolli at the opening ceremony and the lecture by Prof. Arnold Katz at the conference dinner could be considered to be the *cheese* on the pizza. Dr Bolli's talk and Dr Katz's lecture clearly delineated what is important in the transition between molecular and cellular-based experiments and clinical trials.

As *toppings* of our scientific pizza, we had many brilliant selections from over 130 presentations. In particular, new insights into the molecular basis of calcium handling in heart failure and the development of myocardial re-gensis approaches may contribute to interventional therapies to cure cardiovascular disease.

The winner of the Young Investigators Award Competition was Dr Vasant Jayasankar from Philadelphia. The title of his presentation was Adenoviral gene transfer and local overexpression of growth hormone

preserves post infarction myocardial function and ventricular geometry.

Posters were presented during coffee breaks at the area near the hotel entrance. It was nice for poster presen-

ters to have the opportunity to present their data, but there might not have been enough time to discuss their data fully.

This meeting included not only progress reports by each investigator's laboratory but also comfortable and enjoyable lunches and dinners, making this meeting very different from some big scientific meetings such as the American Heart Association. Although the meeting was only a 3-day conference, it definitely provided a good opportunity for young investigators and post-docs to talk to professors on scientific and non-scientific topics. Finally, I believe all attendees could enjoy a juicy delicious scientific "Mystic Pizza" during this meeting!

Kenichi Imahashi, Ph.D.
Durham, NC, USA



Dr Imahashi is discussing his poster 'Transgenic expression of Bcl-2 reduces cytosolic acidification in ischemic myocardium and promotes restoration of creatin phosphate after reperfusion' with (from left to right) Drs Haiyan Tong, Dipak Das (Chairman of the Organizing Committee) and Jim Downey.

THE 2003 JANICE PFEFFER DISTINGUISHED LECTURE

HONORED SPEAKER (MYSTIC, CONNECTICUT): PIERO ANVERSA, M.D. MYOCARDIAL REGENERATION IN HEART FAILURE



DR ANVERSA received his M.D. degree from the University of Parma (Italy) in 1965. He quickly rose to the rank of Professor of Pathology at the University of Parma and subsequently Professor of Pathology, Medicine, and Microbiology and Immunology at New York Medical College, where he is also Vice-Chairman of the Department of Medicine and Director of the Cardiovascular Research Institute.

Dr Anversa's scientific accomplishments have been extraordinary. During his remarkably productive career, he has designed, conducted, and published a large number of seminal studies which have provided fundamental new insights into the pathophysiology of myocardial infarction, ventricular remodeling, heart failure, and cardiac repair. His investigations are uniformly characterized by their thoroughness, comprehensive nature, and technical excellence. Perhaps the most striking feature of Dr Anversa's work, however, is its innovativeness: His studies challenge existing paradigms rather than expanding them, and in so doing they have led to novel ideas that have advanced our understanding of cardiovascular disease. For example, his demonstration that stretch-induced generation of angiotensin II contributes to fibrosis after infarction has paved the way for the use of ACE inhibitors in

patients with heart failure. Despite obstinate recalcitrance in the molecular establishment, Dr Anversa's demonstration that cardiac myocytes can divide *in vivo* has impelled a radical reassessment of the widely-accepted belief that these cells are terminally differentiated. Even more provocative – and far-reaching – are the implication of Dr Anversa's recent studies documenting the ability of hematopoietic and cardiac stem cells to differentiate into cardiac myocytes and other cardiac cell types. These findings have had an enormous impact on the scientific community; more than anyone else's work, they have stimulated the development of the burgeoning field of cardiac regeneration.

Dr Anversa's productivity has been phenomenal. He has published over 200 original articles, many of which have appeared in the most stringent journals (47 in *Circ Res*, 8 in *JCI*, 5 in the *N Engl J Med*, 2 in *Nature*, and 5 in *PNAS*). He has also published 61 book chapters/review articles, is a regular speaker at national and international meetings, and serves as a frequent reviewer for NIH grant and program project applications.

Few other cardiovascular investigators can boast an impact on the scientific community comparable to Dr Anversa's. He is a leader rather than a follower. He does not adapt other

people's ideas to his model – he generates new ideas for others to test and adapt to their models. Through his tenacious (and at times lonely) work, he has reshaped the way we think about such fundamental issues as ventricular remodeling, cardiac cell cycle regulation, hypertrophy, and cardiomyocyte death and regeneration. The hallmark of a great scientist is his/her ability to change prevailing thinking patterns. That, Dr Anversa has certainly done.

The ISHR has recently established the Janice Pfeffer Distinguished Lecture to honor the memory of the late Janice Pfeffer and recognize her contributions to cardiovascular research. This lecture will be held at the World Congress of the ISHR and, in the non-Congress years at the meetings of the North American Section, to which Janice Pfeffer belonged. The topic of this lecture will be in the area of heart failure, hypertrophy, and left ventricular remodeling. The first Janice Pfeffer Lecture was delivered by Piero Anversa at the XXVth meeting of the North American Section in Mystic, CN, on June 30, 2003. Dr Anversa provided a provocative overview of his recent discovery of cardiac stem cells and their role in turnover in cardiac myocytes, regeneration of infarcted myocardium, and rejuvenation of aging myocardium.

INTERNATIONAL SOCIETY FOR HEART RESEARCH AWARDS
The Richard Bing Young Investigator Award, The Research Achievement Award, and
The Peter Harris Distinguished Scientist Award

The International Society for Heart Research (ISHR) has established three very distinguished awards of international importance for recognizing outstanding scientists who have made significant contributions to the advancement of cardiovascular science: The Richard J. Bing Young Investigator Award, the Research Achievement Award, and the Peter Harris Distinguished Scientist Award. While the Richard Bing Award recognizes young talent, the Peter Harris Award focuses on lifelong accomplishments and the Research Achievement Award is targeted at scientists in the intermediate phase of their career. The monetary prize for the Richard Bing Award will be \$5,000, for the Research Achievement Award, \$30,000, and for the Peter Harris Award \$5,000. These high-profile recognitions will be presented at the XVIIIth World Congress of the ISHR in Brisbane, August 7-11, 2004. The winners will be announced in the *Journal of Molecular and Cellular Cardiology* (the official publication of the ISHR), in the ISHR website, and in *Heart News and Views* (the newsletter of the ISHR).

Richard J. Bing Young Investigator Award

- The purpose of this Award is to recognize outstanding research endeavors by new investigators and to encourage continued biomedical research careers.
- Candidates must be less than 36 year-old on August 11, 2004.
- Four finalists will present their work at the XVIIIth ISHR World Congress.
- The winner will receive a plaque and a cash award of \$5,000. The three runner-ups will receive a plaque and a cash award of \$1,000. Travel expenses will be reimbursed up to \$3,000.

Research Achievement Award

Sponsored by Chugai Pharmaceutical Company

- The purpose of this Award is to recognize a scientist who has made major and independent contributions to cardiovascular science and who is likely to further develop his/her research in the future.
- Nominees must be less than 55 year-old on August 11, 2004.
- The winner will receive a plaque and a monetary prize of \$30,000. He/She will present a major lecture at the XVIIIth World Congress of the ISHR.

Peter Harris Distinguished Scientist Award

- The purpose of this Award is to recognize lifetime contributions to cardiovascular science. Its presentation will be a highlight of the XVIIIth World Congress of the ISHR. Previous recipients include S. Ebashi, A. Fleckenstein, R.B. Jennings, H. Morgan, and L. Opie.
- The winner will receive a plaque and a cash award of \$5,000 and will present a major lecture at the XVIIIth World Congress of the ISHR.

Details regarding the procedure for application/nomination for these awards can be found on the ISHR website (www.ishrworld.org, click under "Society Awards").

Please send applications/nominations for the Bing and Harris Awards to **Roberto Bolli, M.D., Secretary General, ISHR**, Division of Cardiology, ACB, Third Floor, University of Louisville, 550 South Jackson Street, Louisville, KY 40202, Phone (502) 852-1837, fax (502) 852-6474, email address: rbolli@louisville.edu. Deadline for receipt of applications/nominations for the Bing and Harris Awards is **January 9, 2004**.

Nominations for the Research Achievement Award should be sent to **James Downey, Ph.D., President, ISHR**, Department of Physiology, University of South Alabama, Medical Sciences Bldg., Rm 3024, Mobile, AL 36688, Phone (251) 460-7004, fax (251) 460-6464, email address jdowney@usmail.usouthal.edu. The deadline for receipt of nominations for the Research Achievement Award is **December 19, 2004**.

ISHR MEETINGS CALENDAR

- **January 9-11, 2004.** Meeting of the Indian Section and the International Academy of Cardiovascular Science. Lucknow, India. **Inquiries:** Dr V.K. Puri, Department of Cardiology, CSM Medical University (Upgraded K.G.'s Medical College), Lucknow-226003 (U.P.) India. Tel. +91 522 2330081 or 2324683; E-mail vijaykumarpuri@hotmail.com
- **May 2-5, 2004.** XXVI American Section Meeting - "Bench to Bedside and Back; Exploring New Paradigms" - A multinational perspective of cardiovascular research in North America. Cancun, Mexico. **Inquiries:** Dr D. Villarreal, Division of Cardiology, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, New York 13210, USA. Tel. +1 315 464 9578; Fax +1 315 464 9571; E-mail villarrd@upstate.edu
- **June 2-6, 2004.** XXIV European Section Meeting. Dresden, Germany. **Inquiries:** Dr U. Ravens, Medical Faculty Carl Gustav Carus, Dresden University of Technology, Fetscherstrasse 74, 01307 Dresden, Germany. Tel. +49 351 458 6251; Fax +49 351 458 6315; E-mail ishr-dresden2004@mailbox.tu-dresden.de; Website www.ishr-dresden2004.de
- **August 7-11, 2004.** XVIII World Congress of the International Society for Heart Research. Brisbane, Australia. **Inquiries:** ISHR 2004 Congress, PO Box 164, Fortitude Valley QLD 4006, Australia. Tel. +61 7 3854 1611; Fax +61 7 3854 1507; E-mail heart2004@ozaccom.com.au; Website www.heart2004.com
- **August 28-September 1, 2004.** XXVI Congress of the European Society of Cardiology. Munich, Germany. **Inquiries:** E-mail webmaster@escardio.org; Website www.escardio.org
- **November 7-10, 2004.** Scientific Sessions of the American Heart Association. New Orleans, Louisiana. **Inquiries:** American Heart Association, Meetings and Councils, 7272 Greenville Avenue, Dallas, TX 75231. Tel. +1 214 706 1543; Fax +1 214 373 3406; E-mail scientificconferences@amhrt.org; Website www.americanheart.org

BRISBANE

(continued from page 9)

THE SATELLITE MEETING IN HONG KONG will be held in the Faculty of Medicine, University of Hong Kong. The new state of the art campus is built along a beautiful hillside on the west side of Hong Kong Island. While affording a casual university setting for intimate interactions, you will also be able to see the beautiful sunset from the conference centre. The campus is within easy reach of hotels and the city centre. You will be able to experience the "City of Life" as Hong Kong is proudly known now. A visit to Victoria Peak in the evening will provide you the spectacular sight of the Hong Kong harbor. A shopping and sightseeing trip to Stanley market will give you a taste of the culture and heritage of Hong Kong.

The meeting will focus on *Endothelial factors and coronary disease:*

New understandings and effects of natural products. Professor Paul Vanhoutte will assemble speakers to discuss the latest developments in endothelial derived factors and vascular biology. Another emphasis will be on the effect of natural products on vascular functions. There will be discussions on new and novel therapeutic targets to appeal to the different interest of the participants. The program will have a variety of presentation formats ranging from plenary sessions to poster presentations for casual exchange of ideas.

There are direct flights from Brisbane to Hong Kong (CX102) or via Singapore (SQ246) and Bangkok (TG984) depending on the airline partnership arrangements. The Hong Kong International Airport is considered to be one of the

most efficient airports and is connected to town by the Airport Express. Leaving Hong Kong will be a breeze as Hong Kong has direct flights to most major cities in the world. Hong Kong is also the gateway to China. Visa and a trip to China can be easily arranged locally. The organizing committee welcomes all participants of the ISHR World Congress to make a stop in Hong Kong to join the satellite meeting. We promise you a stimulating scientific program in the exciting city of Hong Kong. For details, contact ISHR-Satellite@hkucc.hku.hk or visit the website at www.ISHR-satellite.hku.hk.

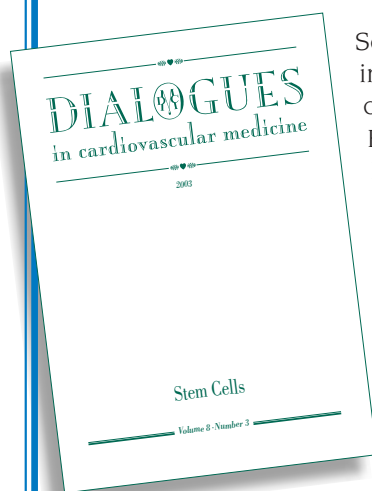
Lindsay Brown, Ph.D.

HEART NEWS AND VIEWS

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Servier supports a number of important projects in the field of cardiology, such as the Education and Training Programs of the European Society of Cardiology.

Servier is also the founding father of The *European Cardiologist Journal by Fax* and *Dialogues in Cardiovascular Medicine*, a quarterly publication with a worldwide circulation edited by

Roberto FERRARI and **David J. HEARSE**.

Dialogues discusses in a comprehensive way issues from the cutting edge of basic research and clinical cardiology.

The forthcoming issue, devoted to
STEM CELLS
will feature articles by:

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H. Reinecke, S. Dimmeler and A. M. Zeiher

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