



# HEART NEWS AND VIEWS

The News Bulletin of the International Society for  
Heart Research

[www.ishrworld.org](http://www.ishrworld.org)

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## Past Truth & Present Poetry

We encounter the name of Doppler when we listen to the weather forecast, or read about the beginning of the universe (the Big Bang, the red shift), or when we study diagnostic reports on heart disease. Who was this man who gave us the tools to explore these divergent subjects? Christian Doppler was born in November 1803 in Salzburg, Austria and died in Venice, Italy on March 17, 1853. He came from a family of master stonemasons and showed exceptional gifts for this craft. But because of his poor health, his father considered him suitable for the bookkeeping function of the family business. But it soon became apparent that Doppler had outstanding talents in mathematics. He was sent to the Polytechnic School in Vienna but he disliked the instructions and called it “a one-sided education”. At the age of 21, he returned to his native Salzburg and finished his education while he supported himself by giving classes in mathematics and physics. He then returned for four years to the Polytechnic in Vienna. Like other great scientists, including Einstein, Doppler received many rejections in response to applications for positions, and finally was compelled to become a bookkeeper. Discouraged, he set his eye on America and in Munich, he discussed with the American consul the possibilities of finding a teaching position in America. He even sold his possessions to finance his journey. But while in Munich, he received two offers to teach in high schools in Switzerland or in Prague, which was then part of the Austrian Empire. These were not university positions but involved high school teaching. Doppler chose the position in Prague, where he again encountered opposition and frustration, making him anxious to leave Prague. Like Einstein who failed to attain an appointment at the technical high school in Zurich, Doppler had an unsuccessful interview for a position at the Polytechnic Institute in Vienna. Interviews with other institutions were equally unsuccessful. In Prague, he published a new



### 14. Doppler and His Principle

optical instrument, called the distometer, for measuring distances and discussed the aberrations of light and sound in a rotating medium. It was at a meeting of the Natural Sciences Section in Prague that Christian Doppler postulated the theory that immortalized his name. He and his family left Prague after he was appointed Professor of Mathematics in a small Czechoslovakian town. Finally, he was elected a Full Member of the Imperial Academy of Science in Vienna and awarded an honorary doctorate from the philosophical faculty. He was then appointed to join the Polytechnic Institute in Vienna and finally, was authorized to found an institute of physics at the Imperial University in Vienna. There, a 20-year-old Augustinian monk, Johann Gregor Mendel, took a written and oral examination to study at the University of Vienna, but Doppler was not very impressed by his mathematical ability and Mendel was refused admission to the university. Mendel was finally admitted. He later laid the foundation of genetics as an abbot in a monastery. Doppler suffered from tuberculosis, which had spread to the larynx and made speaking increasingly difficult. In 1852, his health had so deteriorated that he took a six month period of convalescence in Venice where the climate was supposed to influence the course of tuberculosis. He died in 1853 and was buried in Venice.

Aside from being plagued by ill health all his life, Doppler was continuously afraid of losing his livelihood, with good reasons as his career demonstrates. His friends called him modest, thrifty and correct.

Like many physicists before and after him, he derived his inspiration for his principle from observations of natural phenomena. As he wrote, “We know from general experience that a ship of moderately deep draught which is steering toward the oncoming waves has to receive, in the same period of time, more waves and with a greater impact than one which is not moving or is even moving along in the direction

of the waves. If this is valid for the waves of water, then why should it not also be applied with necessary modification to air and ether waves?" Doppler applied his principle first to astronomy. In his article on the "Colored light of double stars and other constellations of the heavens" he argued that all stars emitted white light and that the color of some of the stars was due to their motion toward us or away from us. Actually this was an erroneous conclusion because on the approach of a star only a slight shift would be produced but no change in color would take place. But the principle is correct; an apparent shift in the frequency of waves received by an observer depends on the relative motion between the observer and the source of the waves. This principle was immediately attacked and as recently as 1965 objections against his principle were published. Others opposed Doppler's theory because of its simplicity. One of them, Petzval, used the argument that, "Without the application of differential equations, it is not possible to enter the realms of great science." Obviously, his critics thought that great truth could not be found in a few lines and through an equation with only one unknown; at least one differential equation is necessary. In 1845, a Dutch scientist, Buys Ballot of Utrecht, confirmed Doppler's principle on the railway between Utrecht and Amsterdam. Using a locomotive capable of attaining the at that time incredible speed of 40 mph, to pull an open cart in which horn players were riding, Ballot attempted to observe changes in the apparent pitch of the notes played by the musicians as they approached or receded. However, the experiment was performed in February and the musicians had trouble blowing their instruments because of the cold, and the project was postponed; in June of that year, the validity of Doppler's theory was finally confirmed.

In cardiology, the principle was first utilized to detect cardiac motion and time the opening and closing of the cardiac valves. Satomura used a con-

tinuous ultrasound beam transmitted through the chest wall to the heart which, reflected from the heart structures underwent a frequency shift, or Doppler shift, of the transmitted sound; its magnitude and direction were based on the speed and direction of movements of the heart. The frequency of the reflected sound was proportional to the velocity of components of the target. Once the velocity of blood flow in the aorta could be recorded, the technique was adapted for measurement of cardiac output. The most important development in cardiac Doppler analysis was the introduction of pulse wave Doppler, which allows localization of flow velocity measurements to specific valves and chambers. It is based on the principle that blood flow in a small area within the heart can be recorded by the use of intermittent pulses of transmitted sound. The receiver then listens for reflected sound only at the end of the time interval required for the pulse to travel from the transducer to the area of interest and back. This way it is possible to localize murmur, determine orifice size from jet diameter, and measure pulmonary flow and pulmonary artery pressure. Doppler's principle has made it possible to determine the ejection fraction of the heart, one of the most valuable measurements in cardiology. It has to a large extent together with echocardiography, replaced cardiac catheterization, particularly in children with congenital heart disease. The correlation between measured Doppler flow velocities and pressure gradients form the basis for assessment of valvular and vascular stenosis, prosthetic valves and permitted estimation of chamber pressure. Simultaneous determination of velocity in several areas of the heart can also be performed. The digitally processed system displays velocity by color-coding. Current instrumentation allows for superimposition of color-coded velocity on the tomography image. Doppler's principle is also applicable to the diagnosis of congenital malformations of the heart in utero.

Christian Doppler's life shows again that scientific accomplishments do not guarantee personal happiness. One of the main reasons in Doppler's case was ill health. Since his early youth, Doppler was plagued by progressive respiratory disease, due to tuberculosis, which involved the larynx. In addition, Doppler's concept was new. Like many great discoveries, it was simple and it was direct. It was just this simplicity and directness which caused other scientists of limited outlook to suspect his principle. Lesser scientists often judge a new discovery by its complexity, which they find attractive. Furthermore, Doppler's discovery had no practical applicability. It took more than 100 years to make an impact on cosmology, meteorology and medicine. As Einstein has said, "Ach der Mensch betrügt sich gern, nimmt die Schale für den Kern" or translated freely "How man does fool himself, mistaking the outer shell for the inner truth."

*Richard J. Bing, M.D.* ■

When Dr Naranjan Dhalla began planning the XVII ISHR WORLD CONGRESS for Winnipeg, Manitoba, Canada July 6 - 11, 2001, he enjoyed amazing success in building The Planning Team. They have made excellent progress in planning an extraordinary Congress. They are blessed with an incredible acceptance by nearly 500 Landmark Lecturers, Speakers and Chairmen to participate. Not only the science but also the social activities will be spectacular.

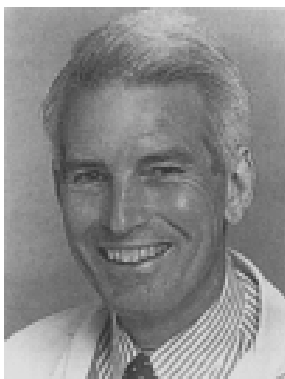
You can now download the complete registration and abstract submission package from:

[www.heartconference.com](http://www.heartconference.com)

We look forward to welcoming you to Winnipeg to explore "FRONTIERS IN CARDIOVASCULAR HEALTH"!

*Dr James Downey*  
*ISHR, President Elect* ■

## PRESIDENT'S LETTER



### Konnichiwa

This news letter is written whilst attending the 17<sup>th</sup> Meeting of the Japanese Section of the ISHR. This year's meeting focuses on Molecular Mechanisms of EC Coupling and is held in Osaka, organised with impeccable efficiency by Professor Michihiko Tada from Osaka University Graduate School of Medicine. The Japanese Section always sets a superb example to the other Sections of the ISHR, firstly by providing an excellent, topical and balanced scientific programme with ample opportunity for young Japanese investigators to present their latest work (see the November 2000 issue of the *Journal of Molecular and Cellular Cardiology*), secondly the Section organises its meeting at the same time every year and thirdly they always recognise the international spirit of the ISHR by inviting a number of foreign speakers to contribute *and* allowing them to speak in English! This year, in addition to myself, Drs M Schneider, D Bers, A Marks, G Hassenfuss, P Pfaffinger, S Sollott and J Molquentin are enjoying the legendary hospitality of our Japanese colleagues.

Stepping off the plane, I was immediately taken to participate in a video recording of a fascinating ISHR roundtable discussion with Professors Hikaru Matsuda and Masatsuga Hori on the problems of cardiac transplantation in Japan. To the frustration of cardiac surgeons and to the cost of many seriously ill patients, heart transplantation has long been prohibited in Japan. This is because the law did not recognise brain death as a legal form of death. As a consequence, the early pioneers of cardiac and renal transplantation rapidly found themselves facing serious charges in court! In 1997, after almost a decade of lobbying, the Japanese Parliament finally passed legislation recognising brain death as a legal sign of death. This paved the way for the opening of two cardiac transplantation centres, both in Osaka. In the past two years 6 transplants have been undertaken with complete success, a small number of cases but an important start. Unfortunately, social attitudes in Japan and restrictions imposed on and by designated donor hospitals means that there is a desperate shortage of donor hearts - despite an aggressive donor card programme. It is hoped that the recording of the special ISHR roundtable discussion on heart transplantation will help raise awareness of this problem for the general public and the medical profession.

Attending a meeting of the Council of the Japanese Section afforded an opportunity to report that the new Fellowship programme of the ISHR was now fully established and that Dr Howard Morgan's Credentials Committee had selected the first group of Founding Fellows of the ISHR. It was a particular pleasure to be able to announce that this recognition had been conferred on a number of eminent Japanese doctors including Professor Yazaki, the current President of the Japanese Section, and Professor Tada, the organiser of this year's meeting in Osaka. Fellowship of the ISHR is a recognition of outstanding research achievement and a full list of the Founding Fellows will be published in the next issue of HEART NEWS AND VIEWS. Details of our ongoing Fellowship programme are available from our Secretary General Roberto Bolli.

Japanese delegates were very interested to hear the latest news about our next world congress in Winnipeg and its various Satellite meetings. This provides a timely opportunity for me to encourage all our members to register for Winnipeg 2001 and submit abstracts of their very best work. Naranjan Dhalla and his team have promised to provide a landmark meeting that we will all long remember (they have also stressed that Olympic Airlines do not fly to Winnipeg!).

Young investigators hoping to attend Winnipeg 2001 should remember that the ISHR Travel Fund will be offering a substantial number of travel bursaries to facilitate attendance at the Congress. Details of these bursaries, which are linked to the submission of outstanding abstracts, are available from the Congress organisers.

The run up to the World Congress is always a busy time for the ISHR and one important activity is the election of a new Council and new Officers. Jutta Schaper's Nominating Committee have now completed their work and an election is currently underway to appoint a number of new Council Members and also identify a President to succeed Jim Downey in 2004. With nominations from Japan, France and Italy it promises to be an exciting

*(continued on page 4)*

election – Roberto Bolli assures me that the votes will *not* be counted in Florida! Fortunately, we do not have to elect a new Secretary General since Roberto (who has proven that he is as superb as a Secretary General as he is as a cardiovascular investigator) has agreed to serve a second term of office – thank you Roberto! Sadly, Tom Ruigrok, who has edited HEART NEWS AND VIEWS since its inception, has indicated that he wishes to hang up his editorial hat and pass the baton to a new editor – news of this appointment will be in the next issue of HEART NEWS AND VIEWS but it is appropriate to thank Tom for his outstanding work over the past few years. I would also like to thank Roberto Ferrari, his long period of service on Council comes to an end in 2001. Roberto, in his post of Treasurer, with Bob Jennings the Chairman of our Finance Committee, has rationalised and revolutionised the management of ISHR resources and sincere thanks go to both of them. Although Roberto Ferrari may be leaving our Council he will continue to offer his enthusiastic help and support in a number of important ways but more of that in future issues of this bulletin!

Recently, the Council of the ISHR agreed to a major structural change such that, from 2001 onwards, all our Sections will have one or more statutory positions on our Council. I believe that this will greatly enhance the influence of our Sections on decisions made by our International Council whilst, at the same time, improving communication between our Sections.

One of the important decisions to be made in Winnipeg will be to identify the venue for our 2007 world congress, to date there are three excellent proposals and it will clearly be a tough decision for our new Council, the Society is fortunate to have so many offers for what, speaking from personal experience, can be a most challenging (and occasionally harrowing) task. The winning proposal will be announced in Winnipeg.

Having mentioned our 2001 and 2007 World Congresses it is appropriate to remind members that our 2004 Congress will be in sunny Brisbane. Lindsay Brown and his team are well ahead of schedule having finalised the congress site, date and the concept of holding the meeting conjointly with the Cardiac Society of Australia and New Zealand. The first announcement is already available and details can also be found on the ISHR website ([www.ishrworld.org](http://www.ishrworld.org)). At last you will have a chance to combine great science with a trip to Australia's Gold Coast! Meanwhile, it's now time to enjoy some more sessions of the Japanese meeting.

**Sayonara**



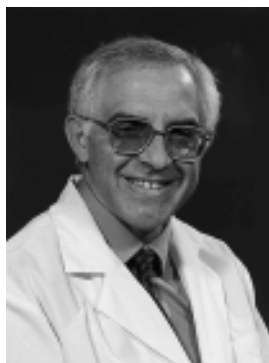
*David J. Hearse*

It is with great sadness that I share the news with our membership that Dr Vincenzo Panagia, M.D., Ph.D., a good friend of the Society, passed away peacefully on November 24, 2000 at the age of 61. Dr Panagia was a Professor of Anatomy and Physiology in the Faculty of Medicine at The University of Manitoba. He was also the Director, Membrane Biology Laboratory, Institute of Cardiovascular Sciences, St. Boniface General Hospital Research Centre.

Dr Panagia came to Winnipeg in 1977 and started out his research in membrane phospholipids. Very soon, he became a leading authority in the study

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## In Memoriam



*Vincenzo Panagia  
1939 - 2000*

of membrane phospholipids and their role in signal transduction in the heart in health and disease. He mentored many graduate students, fellows and visiting scientists.

He is survived by his loving wife Marisa and his two sons, Davide and Marcello. He will be missed dearly by his colleagues and most especially by his students whom he cherished and guided with care. On a personal note, Enzo was a fine colleague; his warmth and the famous smile will always be missed.

*Prof. Pawan K. Singal  
Winnipeg, Manitoba, Canada* ■

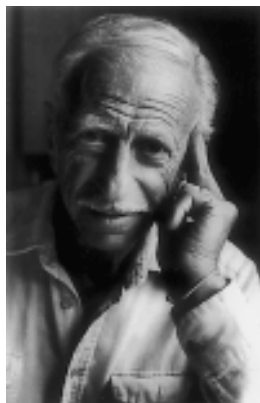
ALBERT WOLLENBERGER, Ph.D., Sc.D., the second President of the International Society for Heart Research, died on 25 September 2000 in Berlin. His friends, former students and colleagues, nationally and, in particular, internationally, will preserve his memory as an outstanding and enthusiastic scientist and a very committed researcher. "Albert was so often one step ahead of us in his thinking" remembered Lionel H. Opie, when the undersigned visited the Cape Town Hatter Institute in November 2000.

Albert Wollenberger was born on 21 May 1912 in Freiburg/Breisgau, Germany. In 1933, for political reasons, he had to leave Germany and remained abroad for over 20 years. Emigrating to the U.S.A., he continued his academic education in Biology and Medical Sciences at Harvard University, Boston (1940-1944), where he obtained his Ph.D. In the fifties, Albert Wollenberger returned to Europe. His research took him to Denmark, Sweden, England and finally to the Humboldt University, Berlin. In 1954, he became a full professor and, in 1956, he founded a Cardiac Research Group at the German Academy of Sciences in Berlin-Buch. He remained head of this institution, later named Department of Molecular and Cellular Cardiology at the Central Institute for Heart and Circulatory Research, for 21 years.

During this period, he was able to make an outstanding contribution to our current understanding of the function and the neuronal and hormonal regulation of the heart. Wollenberger belonged to the first to cultivate isolated beating cardiomyocytes and initiated their biochemical and pharmacological characterization. He made huge contributions to the energy metabolism in the healthy and failing heart, to the mechanism governing the transition from an aerobic to an anaerobic energy supply in the acutely ischemic heart, and he demonstrated the oscillatory

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## In Memoriam



*Albert Wollenberger  
1912 - 2000*

changes in the level of cyclic AMP and cyclic GMP during the beat-to-beat rhythm in frog ventricular heart tissue. The discovery of cyclic AMP-dependent protein kinases led Albert Wollenberger to initiate a research programme aimed at identifying a possible substrate, which might be an intrinsic protein of the sarcolemma or sarcoplasmic reticulum of cardiomyocytes. At that time (1972), his East German group was competing only with American groups to be the first to identify the role of protein phosphorylation in regulating calcium homeostasis and, thereby, contraction and relaxation of the heart.

Right from the very beginning of his research activities, Albert Wollenberger was passionately interested in improving methodological standards to allow future progress. To this end, he developed an ultra-rapid freeze-stop technique which allowed the cryofixation of cardiac tissue. For more than forty years this cryofixation procedure (colloquially referred to as the *Wollenberger clamp*) remained an essential step in all the analytical work involving excitable tissue like the myocardium. Throughout his life, Albert Wollenberger believed that application of the latest advances in basic research would lead to new ways of treating and preventing heart disease. His group detected the

efflux of glycogen phosphorylase from the myocardium following damage induced by ischemia, which afterwards was developed to a very sensitive diagnostic tool for patients with acute myocardial infarction. Furthermore, auto-antibodies to  $\beta_1$ -adrenergic receptors were detected in the blood of patients with severe heart failure and believed to be causally involved in the deterioration of the myocardium (dilated cardiomyopathy).

Albert Wollenberger was one of the founders of the ISHR, under his leadership the Journal of Molecular and Cellular Cardiology was initiated, and he belonged to the editorial board for 19 years. His knowledge and experience in many areas of cardiac research and clinical cardiology also meant that he served on a number of international editorial boards and of Scientific Committees of Conferences and Meetings around the world. Albert Wollenberger was a member of the Royal Society of Medicine, U.K., the American Association for Advancement of Science, and the German Academy of Natural Sciences LEOPOLDINA. At the first conference on the "Physiology and Pharmacology of Cyclic AMP", held in Milan, Italy, in 1971, he was honoured together with the Nobel prize laureate Earl W. Sutherland, for his particular contribution to this rapidly developing area in myocardiology.

*Prof. Ernst-Georg Krause  
Berlin-Buch, Germany* ■



### Welcome to Canada

The International Society for Heart Research is now a truly global organization in meeting future frontiers in cardiovascular medicine and surgery. With its strong member base, the dedication of a few and the commitment of many, the ISHR continues to grow. It holds eight sectional meetings throughout the world each year and its international congress ever three years. During the past 50 years, more progress has been made in the diagnosis, treatment and prevention of cardiovascular disease than had been achieved throughout the history of mankind. A wonderful accomplishment no doubt, but really, the task at hand remains daunting. Heart disease is still the leading cause of death on a global scale, and much work remains.

The Organization Committee takes pleasure in inviting you to attend the XVII ISHR World Congress being held in Winnipeg, Manitoba, Canada in 2001. Your attendance will help ensure that our work carries on and grows; for good science and hard work are keys to helping everyone overcome the seemingly insurmountable hurdles we face.

### The Planning Teams

In July 2001, for the International Society for Heart Research, we expect to create the most important scientific convention ever held in Canada from the point of view of not only numbers of visitors but also the exceptional quality of the people. Over 400 of the World's leading cardiologists, surgeons and scientists have already accepted invitations to participate. The Program will consist of 9 special sessions, 63 Symposia, poster sessions and award competitions. Our targets are professionals involved in Cardiovascular Research, Heart Surgeons, Cardiologists and Academics from as many as 120 countries joined by senior executives from the world's major pharmaceutical and equipment manufacturers. We are planning for 3,500 Delegates, Exhibitors, Graduate Students, Residents and family members. Initial anticipation includes 1,000 Americans (because we have incorporated the annual meeting of the American Section); 800 from Europe (the European Section will also hold their meeting in conjunction with the World Congress); 500 Japanese (including the Japanese Working Group on Cardiac structure and Metabolism); 600 Canadians; and 600 from South America (including their ISHR Section meeting), Asia and Australia. To maximize potential to expose the public to such extraordinary talent, we plan major media support programs through traditional and electronic techniques.

### Proposed Outline of the Scientific Program

#### ■ *Special Programs*

##### □ *Public Forum; "Diet and Exercise for Cardiovascular Health"*

Dr Harvey Finkel, Brookline, USA

Dr Harbans Wasir, New Delhi, India

Dr Bruce Holub, Guelph, Canada

Dr Tom Kottke, Rochester, USA

Dr S. Manchanda, New Delhi, India

##### □ *Senior Investigator Awards*

● Peter Harris Award for Established Investigators (being selected by ISHR Council)

● Research Achievement Award (being selected by ISHR Council)

● Special award for Promoting Cardiovascular Education and Research (International Academy of Cardiovascular Sciences)

##### □ *Young Investigator Awards*

● Richard Bing Young Investigator Award Competition (4 speakers being selected by ISHR Council)

● ISHR-American Section Young Investigator Award Competition (4 speakers being selected by ISHR-American Section)

● ISHR-European Section Young Investigator Award Competition (4 speakers being selected by Council of ISHR-European Section)

- *12 Cardiovascular Landmark Lectures*
- *340 Symposia Speakers*
- *116 Chairmen*
- *At least 1,000 Posters*

Topics to be covered with respect to etiology mechanisms, pathogenesis and therapeutics: **1** Hypertension, **2** Cardiac hypertrophy, **3** Heart failure, **4** Cardiomyopathies, **5** Myocardial infarction, **6** Atherosclerosis, **7** Thrombosis, **8** Arrhythmias, **9** Restenosis, **10** Vascular disease, **11** Cardiac development, **12** Neointimal hyperplasia, **13** Endothelial dysfunction, **14** Ageing heart, **15** Transplanted heart, **16** Reperfusion injury, **17** Oxidative stress, **18** Apoptosis and necrosis, **19** Acute coronary syndrome, **20** Innovative procedures.

### Abstracts

Abstracts must identify presenter and include registration fee. Must be completed on official form or through Congress web site. Deadline: March 15, 2001.

### Registration Details (all funds in US\$)

	<b>Before March 15</b>	<b>March 16 - June 15</b>	<b>After June 15</b>
ISHR Member	\$350	\$400	\$450
Non-members	\$450	\$500	\$550
Nurses / Students / Fellows / Research & Technical Staff	\$250	\$275	\$300
Accompanying persons	\$200	\$225	\$250

Registration includes: Opening Reception July 6; Banquet July 9; Farewell Dinner July 11; 4 Lunches; Coffee Breaks during Sessions; Congress Material; Access to Scientific Sessions.

**Naranjan S. Dhalla**  
*Congress Chairman*

**Robert E. Beamish**  
*Honorary President*

**Pawan K. Singal**  
*Organization Secretary*

**Grant N. Pierce**  
*Scientific Secretary*

**Ivan Berkowitz**  
*Congress Coordinator*

See also the **MEETINGS  
CALENDAR** on page 11



*Canadian mountie promoting the Winnipeg Congress at the American Heart Association meeting in New Orleans, November, 2000*

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## The ISHR - European Section / SERVIER Research Fellowship

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THE EUROPEAN SECTION of the International Society for Heart Research and SERVIER invite submissions for the first ISHR-ES / SERVIER Research Fellowship. The purpose of this Fellowship is to support the initiation and development of scientific collaborations between outstanding groups in the field of cardiovascular biology by providing a young investigator from a European laboratory with one-year post-doctoral support allowing him/her to carry on a research program in another European country. The term European refers not only to the countries of the European Community but to all countries belonging to the European Section of ISHR.

*Details of the competition are as follows:*

1. Candidates must be members (or have applied for membership) of the ISHR-ES (membership application forms are available at the ISHR-ES web site [www.biomed.cas.cz/fgu/ishr\\_es/](http://www.biomed.cas.cz/fgu/ishr_es/) or can be obtained from Dr Frantisek Kolar, Secretary of the ISHR-ES, Institute of Physiology, Academy of Sciences of the Czech Republic, Videnska 1083, 142 20 Prague 4, Czech Republic. *Tel.* +420 2 475 2559; *Fax* +420 2 475 2125; *E-mail* kolar@biomed.cas.cz).
2. Candidates must have defended their Ph.D. thesis not earlier than January 1, 1999 and be less than 35 years of age on July 1, 2001.
3. Applications must include the following:
  - Curriculum vitae (family name, first name, date of birth, current employment and position, summary of previous positions, degrees, special area of interest and expertise, other activities, publications);
  - Research program of a maximum of 10 pages (including a one page summary and references) detailing the research program (title, aims, rationale, working hypothesis, scientific expertise of each group, preliminary results if any, plan of investigation detailing the scientific procedures and role of each investigator of each group and the precise role of the candidate in the proposed program and funding);
  - Letters of the candidate's current immediate supervisor and future immediate supervisor (Division Heads, Department Chairmen, or Institute Directors) detailing why the collaboration between the two research groups is essential for the success of the research program and why, among all other potential applicants, the applicant is the most appropriate candidate for the Fellowship, and offering a rationale for their opinion.
4. Eight copies of the application should be received by Dr Jean-Jacques Mercadier, President of the ISHR-ES, Departments of Physiology and Cardiology and INSERM U460, Groupe Hospitalier Bichat – Claude Bernard, 46 rue Henri Huchard, 75877 Paris cedex 18, France, **no later than March 30, 2001. Applications received after this deadline will not be considered.**
5. The two collaborating research groups can submit only one application.
6. The applications will be reviewed in Paris in May 2001 by a committee composed of five members of the ISHR-ES Council and one representative of SERVIER. The three best applications will be classified. The second and the third will receive a one-year free electronic subscription to the *Journal of Molecular and Cellular Cardiology*.
7. The winner of the Fellowship will receive a travel grant to cover economy airfare and other travel costs up to 2,500 Euro towards his/her attendance at the XVII World Congress of the ISHR in Winnipeg, July 6-11, 2001. At the Congress, the winner will present his/her research program to the Society. He/she will receive a plaque and check of 20,000 Euro as a personal support. Any winner who, for any reason, cannot personally present his or her research program at the Congress must withdraw from the competition. Substitute presenters are not allowed.
8. It is expected that the results of the investigation will be presented by the recipient at the annual ISHR-ES Congress in Strasbourg, France, in 2003.
9. Applications will not be returned.

*Jean-Jacques Mercadier, M.D., Ph.D.*  
*President, ISHR European Section*

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## Making and Breaking an Embryonic Heart

**Congenital heart defects are the most common birth defect in man - occurring in nearly 1% of all live births and 10% of all stillbirths. My laboratory research interests center on the embryonic and fetal processes that underlie both normal and abnormal heart development in order to understand the origin of clinically important birth defects. The ultimate goal is to develop new therapeutic methods that can prevent the development of these lethal congenital deformities. In particular, we are investigating conotruncal and ventricular septal (“hole-in-the-heart”) defects, cardiac neural crest cell morphogenesis and cardiac neural crest cell-related defects.**

Conotruncal heart defects are important human congenital heart defects that result from a failure of the aorta and pulmonary trunk to become separate vessels from each other during embryonic development.<sup>1</sup> An inadequate number of cardiac neural crest cells colonizing the outflow tract results in the failure of normal formation of a separate aorta (which transports oxygen-rich blood to the body) and pulmonary trunk (which takes de-oxygenated blood back to the lungs). The aim of my work has been to characterize a genetically-defined mammalian mouse model of this disorder. By studying this heart defect in the *splotch* ( $Sp^{2H}$ ) mutant mouse model – called the *splotch* ( $Sp^{2H}$ ) because of the white splotch on its belly – (which has a mutation in the DNA-binding homeodomain of the *Pax3* transcription factor), and we have previously shown that *in utero* lethality is due to the conotruncal heart defect<sup>2,3</sup> and that the cardiac neural crest cells (which specifically express *Pax3*) fail to migrate into the developing heart.<sup>4</sup> Thus our previous studies, published in 1997 in the journal *Development*, showed that cardiac neural crest cells never arrived in the *splotch* ( $Sp^{2H}$ ) heart and thus prompted us towards the current study to try to determine why not. Cardiac neural crest cells have to leave the neural tube, migrate through a variety

of different tissues, find their way to the outflow track of the heart, then give rise to the septum – so the ‘black box’ was what happened between the neural tube and the heart.

Our recent results using our *splotch* ( $Sp^{2H}$ ) mouse model to trace in early fetal development the steps of normal septation or formation of the two vessels, which were presented at the 22<sup>nd</sup> meeting of the ISHR (American Section) in Louisville Kentucky (June 14-18, 2000), demonstrated that it is abnormal neural crest stem cell expansion that is responsible for the conotruncal heart defects within the *splotch* ( $Sp^{2H}$ ) mouse mutant.<sup>5,6</sup> Therefore the abnormalities within *splotch* ( $Sp^{2H}$ ) embryos occurred very early in development, before the heart had really been formed or had even started beating, as neural crest stem cells prepared to leave the neural tube – a starting point for cells that will eventually form key structures such as the spinal cord, brain and heart.

Stem cells or progenitor cells needed for development of key blood vessels of the heart do not form normally (not enough of them are specified) in these *splotch* ( $Sp^{2H}$ ) mutant fetuses, resulting in insufficient cardiac neural crest cells colonizing the outflow tract; there simply weren't enough of them to do the job. We are now taking the research back one more step in time to find why



Simon J. Conway, Ph.D.

there aren't enough stem cells. We are working out what is controlling the development and formation of these neural crest stem cells to see if we can determine the primary cause that gives rise to their deficiency and ultimately the heart defect. If there is a way we can artificially give rise to more of these stem cells, we may be able to rescue the heart defects in the mouse embryos, and then possibly apply that knowledge to the clinic.

We have also been putting other mouse models that have conotruncal heart defects through the same analytical steps to see where their heart defects begin. We are looking at several developmental windows when these defects occur, and trying to determine whether there is one common pathway that leads to this heart defect or are there lots of different pathways? My guess is there will be multiple pathways leading to the same serious heart defect, primarily because birth defects in general are multifaceted. However, I think it's important to identify each point at which the defect can occur so that methods can be explored to intervene at the trouble site or sites, potentially thwarting the defect. If you can see where the heart defect first arises and normal development goes awry, you

Dr S.J. Conway was the winner of the Young Investigators Award competition at the XXII American Section Meeting (Louisville, Kentucky; June 14-18, 2000).

could have different therapies to circumvent it and prevent/cure the defect.

I was very pleased, proud and honored to have won the 2000 Young Investigators Award from the ISHR (American Section), and I am greatly indebted to all the present and past members of all the laboratories I've worked in and to the great faith and training that I received as a graduate and post-doctoral student. My initiation into the complicated (and ultimately fascinating) world of the developing mammalian embryo, was as a Ph.D. student with Prof. Anne McLaren (Fellow of the Royal Society) in the Medical Research Council Mammalian Development Unit at University College London in England. After receiving excellent training, the understanding that hard work is required to get results and a Ph.D. in Genetics in 1993, I joined Prof. Andrew Copp's laboratory in the Institute of Child Health at Great Ormond Street Children's Hospital in Central London. My post-doctoral experience (funded by the British Heart Foundation) with Prof. Andrew Copp introduced me to the even more complicated world of the developing mammalian embryonic heart and the study of congenital birth defects. Andy's support, knowledge, style and leadership qualities made a very profound impression on me and I as soon as I started my own laboratory – I tried to adopt the same passion and purpose I'd seen Andy display. While a post-doctoral fellow, I had the great fortune to find myself on the next laboratory bench to Prof. Margaret "Peggy" Kirby (who heads the Heart Development Group at the Medical College of Georgia), who was doing a sabbatical within the Developmental Biology Unit at the Institute of Child Health. Surprisingly, Peggy wasn't distracted by my frenetic working practices in the laboratory and invited me to visit the Medical College of Georgia for three months and to collaborate on our mutual interest in cardiac neural crest cells (and to stay in her attic). After a very positive experience in Augusta Georgia, I moved to the

Medical College of Georgia to start my own laboratory in 1996. Things have gone well in the laboratory and we have been fortunate to be funded by National Institutes of Health, March of Dimes Birth Defects Foundation and the American Heart Association. Winning the ISHR Young Investigators Award has not only personally given me added enthusiasm and drawn attention to our research group, but it has also reaffirmed to my entire laboratory the belief that the work we are doing is noticed, worthwhile and hopefully will ultimately reduce the effects and incidence of congenital heart malformations.

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Simon J. Conway, Ph.D.  
Augusta, GA, USA

## News from the Chinese Section

The Sixth Meeting of the ISHR - Chinese Section was held in Nanjing from October 16–19, 2000. Fifty four of a total of 219 submitted papers were accepted and presented during the meeting. Special lectures included: "Large artery and coronary compliance in health and disease" by Dr A.M. Dart from the Baker Medical Research Institute, Australia; "Studies on heart development in normal and cardiac mutant axolotls, *Ambystoma Mexicanum*, using cellular and molecular biology" by Dr L.F. Lemanski from the University of Tennessee, USA; "Progress on the study of heart failure in transgenic mice" by Dr Du Xiaojun from the Baker Medical Research Institute, Australia; "Contractile protein troponin I: physiological roles in cardiac function and its gene regulation during heart development" by Dr Huang Xupei from the University of Tennessee, USA; " $G_{\beta\gamma}$  protein: its function in the cardiovascular interactive message transduction" by Prof. Yu Xiyong from the Guangdong Cardiovascular Research Institute; and "Biological function of heat shock transcriptin I using gene-depletion model in mice" by Prof. Xiao Xianzhong of the Hunan Medical University. These lectures attracted a great deal of interest and led to heated discussions.

Eight papers were selected from those submitted by young scholars, and three were honoured with the Lu & Yang Award (a special award of the Chinese section for young investigators). "The study on heterogenic coexpression of human ApoA1 and LCAT genes induced by RV in skelomyocytes of mice" by Yu Shuzhen from the Arteriosclerosis Research Institute at Nanjing Medical University got the second prize. Xiao Weiming from the Pathophysiology Department at Hunan Medical University, and Zhou Junling from the Pathophysiology Department at Hebei Medical University won a third prize for their papers "The protective function of  $\alpha\beta$ -

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## ISHR MEETINGS CALENDAR

■ April 29-May 2, 2001. **Israeli Group for Heart Research** (Subsection of the European Section): "**Between Angiogenesis and Heart Failure: 30 Years of Dedicated Research**". Caesarea, Israel. **Enquiries:** Dr G. Kessler-Icekson, The Felsenstein Medical Research Center, Beilinson Campus, Petah-Tikva 49100, Israel. *Tel.* +972 3 921 5228; *Fax* +972 3 921 1478; *E-mail* icekson@post.tau.ac.il

■ July 6-11, 2001. **XVII World Congress of the International Society for Heart Research.** Winnipeg, Manitoba, Canada. **Enquiries:** XVII ISHR World Congress, c/o Institute of Cardiovascular Sciences, St. Boniface General Hospital Research Centre, University of Manitoba, Faculty of Medicine, 351 Taché Avenue, Winnipeg, Manitoba, Canada R2H 2A6. *Tel.* +1 204 235 3421; *Fax* +1 204 233 6723; *E-mail* ishr@cc.umanitoba.ca; *Website* www.heartconference.com

■ July 2-5, 2001. **Regulation of Energy Metabolism in the Heart and Vasculature.** Banff, Canada. **Enquiries:** Dr G.D. Lopaschuk, c/o Cardiovascular Disease Research Group, Department of Pediatrics, University of Alberta, 423 Heritage Medical Research Centre, Edmonton, AB, Canada T6G 2S2. *Tel.* +1 403 492 2170; *Fax* +1 403 492 9753; *E-mail* gary.lopaschuk@ualberta.ca

■ July 3-5, 2001. **Heart Failure Summit.** Toronto, Canada. **Enquiries:** Dr M.J. Sole, c/o The Centre for Cardiovascular Research, Eaton Wing 13 North - Suite 208, Toronto General Hospital, Toronto, ON, Canada M5G 2C4. *Tel.* +1 416 340 3471; *Fax* +1 416 340 5985; *E-mail* mssole@torhosp.toronto.on.ca

■ July 12-15, 2001. **Diseases of the Cardiovascular System and Immunity: Interactions and Therapeutics.** Montreal, Canada. **Enquiries:** Dr G. Bkaily, c/o Department of Anatomy and Cell Biology, Faculty of Medicine, University of Sherbrooke, 3001 12E Avenue North, Sherbrooke, PQ, Canada J1H 5N4. *Tel.* +1 819 564 5303; *Fax* +1 819 564 5320; *E-mail* g.bkaily@courrier.usherb.ca

■ July 12-15, 2001. **Remodeling and Progression of Heart Failure.** Minneapolis, USA. **Enquiries:** Dr I. Anand, c/o Department of Cardiology, VA Medical Center 111C, 1 Veterans Drive, Minneapolis, MN, USA 55417. *Tel.* +1 612 725 2000, ext. 3723; *Fax* +1 612 725 2262; *E-mail* anand001@maroon.tc.umn.edu

■ July 13-17, 2001. **International Muscle Energetics Conference.** Burlington, USA. **Enquiries:** Dr N.R. Alpert, c/o Department of Physiology & Biophysics, University of Vermont, College of Medicine, Given Medical Building, Burlington, VT, USA 05405-0068. *Tel.* +1 802 656 2540; *Fax* +1 802 656 0747; *E-mail* alpert@salus.med.uvm.edu

■ September 2-4, 2001. **Models in Cardiovascular Research (Australasian Section) - Satellite Meeting of the IUPS 2001 Congress.** Brisbane, Australia. **Enquiries:** Satellite Meeting Secretariat, PO Box 164, Fortitude Valley QLD 4006, Australia. *Tel.* +61 7 3854 1611; *Fax* +61 7 3854 1507; *E-mail* IUPS@ozacom.com.au; *Website* www.baker.edu.au/ISHR

■ July 3-6, 2002. **XXII Meeting of the European Section.** Szeged, Hungary. **Enquiries:** Dr A. Végh, Department of Pharmacology and Pharmacotherapy, University of Szeged, Faculty of Medicine, Dóm tér 12, H-6720, Szeged, Hungary. *Tel.* +36 62 545 673; *Fax* +36 62 544 565; *E-mail* vegh@freemail.hu; *Website* www.cardiovasc.com/ishr2002

■ August 7-11, 2004. **XVIII World Congress of the International Society for Heart Research.** Brisbane, Australia. **Enquiries:** ISHR 2004 Congress, PO Box 164, Fortitude Valley QLD 4006, Australia. *Tel.* +61 7 3854 1611; *Fax* +61 7 3854 1507; *E-mail* heart2004@ozacom.com.au; *Website* www.baker.edu.au/ISHR

### *In Blue: XVII World Congress and Satellite Meetings*

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lens protein in the early phase and delayed phase of myocardial preconditioning" and "The effect of HO-I-CO signal system on pulmonary lesion induced by reperfusion after acroischemia and its relationship with NO", respectively. The first prize was not awarded.

During the business meeting Prof. Han Qide was re-elected as President, Prof. Wu Liling was elected as Secre-

tary, Prof. Gao Guangdao as Vice-president, and Prof. Wu Liling as Treasurer. It was decided that the headquarters of the Section will continue to be located at the Peking University Health Sciences Center (formerly Beijing Medical University).

The participants also discussed the future activities of the Section. They unanimously agreed that the coopera-

tion between researchers should be reinforced, and that priority should be given to integrate the activities of the Section with other academic societies, as well as to engage clinical cardiovascular practitioners to improve the quality and efficacy of future symposia.

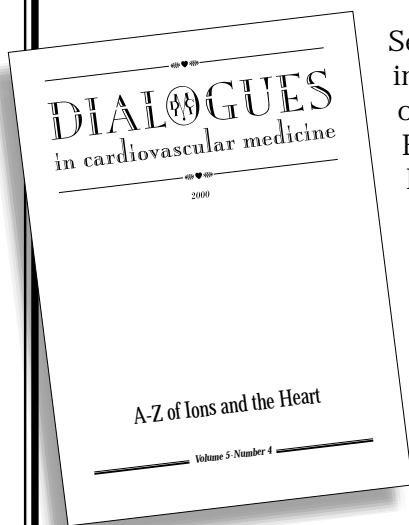
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## HEART NEWS AND VIEWS

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Heart Lung Institute (Room G02.523),  
University Hospital, Heidelberglaan 100,  
3584 CX Utrecht, The Netherlands.  
Tel.: +31 343 597 555  
Fax: +31 343 597 510  
E-mail: t.j.c.ruigrok@xs4all.nl