The International Society for Heart Research (ISHR) was started in Boston in 1967 as the International Study Group for Research in Cardiac Metabolism (Study Group). The Study Group was founded by Dr Eörs Bajusz (Boston) in collaboration with Drs Richard Bing (Pasadena) and George Rona (Montreal), and was registered with appropriate by-laws and logo (Fig. 1A) as a Non-Profit Organization in the Commonwealth of Massachusetts in 1967. The objectives of this organization were to: (i) promote research in cardiac metabolism, structure and function; (ii) disseminate knowledge in cardiac sciences; and (iii) foster research collaborations through publications, conferences and other media. Several experimental and investigative cardiologists from USA and Europe were invited to become Founding Members effective 1968 (Table 1). While Dr Bajusz assumed the office of Director of International Affairs, Dr Bing agreed to serve as President, Dr Edward Sonnenblick...
Table 1. Founding Members of the International Study Group for Research in Cardiac Metabolism (1968).

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abelman WH, Boston, USA</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Bajusz E, Boston, USA</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Baroldi G, Milan, USA</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Bing RJ, Pasadena, USA</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Bloor CM, La Jolla, USA</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Brachfeld N, New York, USA</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Brink AJ, Bellville, South Africa</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Buja LM, Bethesda, USA</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Burn CF, New Orleans, USA</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Cantin M, Montreal, Canada</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Carafoli E, Zurich, Switzerland</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Carmeliet E, Leuven, Belgium</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Caullfield J, Boston, USA</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Dhalla NS, Winnipeg, Canada</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Ferrans VJ, Bethesda, USA</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Fleckenstein A, Freiburg, Germany</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Goodwin JF, London, England</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Gudbjarnason S, Reyjavík, Iceland</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Harris P, London, England</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Hatt PY, Paris, France</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Hess ML, Richmond, USA</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Jennings RB, Chicago, USA</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Katz AM, New York, USA</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Krause EG, Berlin-Buch, Germany</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Kubler W, Dusseldorf, Germany</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>Lockner A, Bellville, South Africa</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>Moret P, Geneva, Switzerland</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Opie LH, London, England</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Olson RE, St. Louis, USA</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>Ostadiel B, Prague, Czechoslovakia</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Poupou O, Prague, Czechoslovakia</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Raab W, Burlington, USA</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>Regan TJ, Newark, USA</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>Reuter H, Bern, Switzerland</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>Roberts WC, Bethesda, USA</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>Rona G, Montreal, Canada</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>Schwartz A, Houston, USA</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>Scholoz H, Maine, Germany</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>Schreiber SS, New York, USA</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>Selye H, Montreal, Canada</td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>Shipp JC, Gainsville, USA</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>Sonnenblick E, Boston, USA</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>Spérelakis N, Charlottesville, USA</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>Trautwein W, Hamburg, Germany</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>Vassort G, Orsay, France</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>Williamson JR, Philadelphia, USA</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>Wollenberger A, Berlin-Buch, Germany</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>Zak R, Chicago, USA</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Officials of the Study Group (1968-1976).

<table>
<thead>
<tr>
<th>Year</th>
<th>President</th>
<th>Vice-President</th>
<th>Secretary</th>
<th>Director of International Affairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1968-1970</td>
<td>Richard Bing (Pasadena)</td>
<td>Edward Sonnenblick (Boston)</td>
<td>Arnold Schwartz (Houston)</td>
<td>Bajusz (Boston)</td>
</tr>
<tr>
<td>1970-1972</td>
<td>Richard Bing (Pasadena)</td>
<td>Edward Sonnenblick (Boston)</td>
<td>Arnold Schwartz (Houston)</td>
<td>Bajusz (Boston)</td>
</tr>
<tr>
<td>1972-1973</td>
<td>Richard Bing (Pasadena)</td>
<td>Naranjan Dhalla (Winnipeg)</td>
<td>James Caullfield (Boston)</td>
<td>Bajusz (Boston)</td>
</tr>
<tr>
<td>1973-1976</td>
<td>Albert Wollenberger (Berlin-Buch)</td>
<td>Naranjan Dhalla (Winnipeg)</td>
<td>James Caullfield (Boston)</td>
<td>Bajusz (Boston)</td>
</tr>
</tbody>
</table>

Dr. Eörs Bajusz (Fig. 1B) was a highly talented individual with clear vision, great intellect and exceptional organizational skills. In 1968, he persuaded a German pharmaceutical company to host the first International Congress of the Study Group in the beautiful city of Dubrovnik (former Yugoslavia). In the same year, he started discussions with Academic Press, London to publish the proceedings of different Congresses of the Study Group in the form of a series of books, “Recent Advances in Studies on Cardiac Structure and Metabolism”, edited by Dr Bajusz in collaboration with Dr Rona.

The Bajusz/Bing/Rona team next identified appropriate individuals for 2-year appointments as Council Members to govern the organization (Table 3). Furthermore, Dr Bajusz persuaded his personal friends, namely, Drs G. Baroldi (Milan), A.J. Brink (Bellville) and W. Raab (Burlington), to organize and chair International Congresses in Italy, USA and South Africa in 1969, 1970 and 1971, respectively. From 1971 to 1976, the Study Group underwent several organizational alterations, including expansion of its scope and activities and promotion of worldwide membership. Thus in 1976 the name of the Study Group was changed to the International Society for Heart Research (ISHR) at the 8th International Congress in Tokyo to better reflect the diverse expertise of its membership. New by-laws were developed by Dr Robert B. Jennings (Durham) to govern the ISHR and define the relationship between different international Sections (Jennings RB, Heart News and Views, 18:3, 2011). These by-laws were approved in 1980 at the International Congress in Moscow (Journal of Molecular and Cellular Cardiology 24: 1203-1210, 1992), and ISHR was registered and incorporated as a Non-Profit Organization under the Canadian Incorporation Act in 1982. The current ISHR logo (Fig. 1C), proposed by Dr Judta Schaper (Bad Nauheim), was adopted at the International Congress in Prague in 1995.

Development of Different Sections

While preparations for the 1974 International Congress held in Quebec City, Canada were in progress, it was decided to hold all future Congresses every two years instead of annually. This was done to accommodate the proposal of some European members, who wished to set up a European
Section of the Study Group to hold meetings in Europe in the alternate years. This proposal was approved by the Council and ratified at the General Assembly in Freiburg in 1973. The Executive Committee, including Drs Bing, Wollenberger, Rona and Dhall, continued to promote membership and cardiovascular activities in other parts of the world, leading to the formation of the American, Japanese, Indian, Soviet and Australasian Sections between 1973 and 1978 (Table 4). When the name of the Study Group changed to ISHR in 1976, all the Sections of the Study Group were renamed as ISHR-Sections. The ISHR-East European Subsection was established in 1981, and the ISHR-Latin American and ISHR-Chinese Sections were formed in 1983 and 1984, respectively. Each Section has a history of its own, and a brief account of the structure and development of each Section will be presented in a future issue of the newsletter.

**Organization of International Congresses**

All Chairs of the 16 international Congresses held between 1968 and 1998 (Table 5) had a strong commitment to promoting cardiovascular science; however, each of these individuals had their own style in the selection of scientific program and delivery of their content, and thus made a unique impact on the participants. The attendance at the first four Congresses at Dubrovnik, Gargnano, Stowe and Tiervlei varied between 40 to 150 whereas the Prague Congress registered more than 1,200 participants. The increased attendance over time at these Congresses reflected the growth and popularity of the ISHR. It was a great honor to Chair an ISHR Congress, and the Council invariably had to make a difficult decision in selecting the successful proposal. The organization of a Congress was not an easy task as one has to raise funds for all expenditures and assemble committees for scientific program, administration, hospitality, and entertainment.

Each Congress was expected to achieve several objectives: (i) holding several symposia sessions on cutting-edge cardiovascular science; (ii) exchanging information and ideas for new lines of investigation to find solutions for diverse and complex research problems; (iii) providing opportunities for networking and developing research collaborations; (iv) holding Council meetings to discuss the past, present and future operations of the organization, and (v) convening the General Assembly for the ratification of elections and other decisions of the Council by the membership at large. Each Congress engendered its own excitement and was a venue for developing long lasting relationships and friendships among the participants. The organizers of each Congress arranged high quality, enjoyable social programs to showcase their hospitality, pride and commitment. Social events during the celebration of the 25th Anniversary of ISHR in Kobe, Japan were indeed a memorable celebration of the 25th Anniversary of ISHR, publication of JMCC and the remarkable success and strength of ISHR. ISHR is the flagship of this organization. The remarkable success and strength of JMCC over the years can be attributed to its Founding Editors,

**Publications and Conference Proceedings**

Although organizing meetings with high quality scientific programs is a major function of ISHR, publication of JMCC is the flagship of this organization. The remarkable success and strength of JMCC over the years can be attributed to its Founding Editors,
Drs Bing and Opie, but it is also important to acknowledge the contributions of Academic Press in publishing this high impact journal. Although JMCC was started as an associated project of the Study Group/ISHR in 1970 and did not become the official journal of ISHR until 1981, all members of its Editorial Board were appointed by officials of this organization from 1970-1998. In addition to Drs Bing and Opie, two other individuals, Drs Arnold M. Katz and Norman R. Alpert, served as early Editors of the Journal (Table 6) and thus guided its development from 1987 to 1998.

During the early stages of formation of the Study Group/ISHR, it was decided to publish the proceedings of the Congresses for the benefit of those who were unable to participate. Accordingly, several Book Series, “Recent Advances in Studies on Cardiac Structure and Metabolism” (1972-1978) and “Advances in Myocardiology” (1980-1985) were published by the University Park Press, Baltimore as well as the Plenum Medical Company, New York. The books contain review articles and original research papers and represent a true historical record of cardiovascular research during the 15 years of the development of ISHR. In 1992, the ISHR Council initiated the publication of a quarterly bulletin, “Heart News and Views”, under the editorship of Dr Thomas Ruigrok, for promoting communication among the members and Sections of the organization. These publications have enhanced the profile of ISHR as a global institution.

(continued on page 15)
The 2019 World Congress in Beijing is only a little more than a year away. The World Congress, organized by Dr. Yi Zhu, President of the Chinese Section, will be held June 3 to 6th in the Chinese National Convention Center (CNCC) in Beijing. Planning for the ~25 ISHR-sponsored symposia is underway. In response to a request for proposals, the membership submitted 91 symposium proposals which included 259 unique speakers. It will be a difficult job for the Scientific Program Committee (SPC) to select the final 25 symposia. The initial review process will be done by 7 Topic Groups: Cardioprotection; Cardiac Dysfunction; Ion Channels and Arrhythmia; Signaling, Disease and Therapy; Beyond the Genome; Regenerative Medicine; and Cardiac Metabolism. Each of the 7 Topic Groups has 2 Co-Chairs and 5 additional members. The Topic Groups will rank and blend the symposia and submit roughly the top 50% to the SPC. The 15 member SPC is chaired by the Secretary General, Lea Delbridge, and composed of the two Co-Chairs of each topic groups: Asa Gustafsson and Derek Hausenloy (Cardioprotection); Jolanda Van der Velden and Martin Vila Petroff (Cardiac Dysfunction); Livia Hool and Anna Maria Gomez (Ion Channels and Arrhythmia); Burns Blaxall and Tetsuji Miura (Signaling, Disease and Therapy); Tom Vondriska and Issei Komuro (Beyond the Genome); Huang Tian Yang and Joe Wu (Regenerative Medicine); and Rong Tian and Rui-Ping Xiao (Cardiac Metabolism). We appreciate the hard work of the SPC in taking on this important task for the ISHR.

An international group of Early Career Investigators (ECIs) is also hard at work planning a symposium and other ECI events for the World Congress. The ECI Committee is composed of two representatives from each section: Kate Weeks and Helen Viola from the Australasian Section, Shimizu Takeshi and Nakagawa Hitoshi from the Japanese Section, Chen Gao and Randi Parks from the North American Section, Delphine Mika and Alessandra Ghigo from the European Section, Junjie Xiao and Ai Ding from the Chinese Section and Luis Gonano and Zully Pedrozo from the Latin American Section (representatives from the Indian Section will soon be appointed). In addition to planning activities at the World Congress this group will liaise with ECIs in their Section to keep them informed. Litsa Kranias and Johannes Backs are serving as advisors to the group. As a first order of business, the ECI group elected Kate Weeks as Chair and Chen Gao as Co-Chair.

In addition to planning ECI symposia and social events for the World Congress, they are making plans for a travel bursary to provide travel funds for ECIs to visit labs in China in conjunction with the World Congress to learn techniques or initiate collaborations. We thank this amazing group of ECIs for all their work! It is also worth mentioning that the ISHR will again fund travel awards for ECIs to attend the World Congress in China.

Lastly, as I mentioned previously, this is the 50th Anniversary of the founding of the ISHR. We are planning a special celebration for the World Congress next year. Dr. Naranjan Dhall, one of the founding fathers of the ISHR, has written a very comprehensive history of the early years of the ISHR. The initial installment of this history is included in this issue of Heart News and Views (p 1-4).

Elizabeth Murphy, Ph.D.
President, ISHR
REPORT ON THE AUSTRALASIAN SECTION MEETING
(AUGUST 10-13, 2017; PERTH, AUSTRALIA)

The 41st annual International Society for Heart Research (ISHR) meeting was held in conjunction with the Cardiac Society of Australia and New Zealand (CSANZ) meeting in Perth, Western Australia. The conference started off with the RT Hall Lecture presented by Prof Stefan Neubauer (University of Oxford), demonstrating masterful application of Cardiovascular Magnetic Resonance (CMR) imaging and spectroscopy, both clinically and experimentally. Prof Robert Graham (Victor Chang Cardiac Research Institute) presented the Kempson Maddox Lecture, titled ‘The mysteries and enigma of spontaneous coronary artery dissection’, and Prof Murray Esler (Baker Heart and Diabetes Institute) delivered the Basic Science Lecture: a highly informative lecture on sympathetic nervous system activation in hypertension. These lectures were a fitting representation of the fundamental research showcased at the conference by a range of ISHR scientists. Topics covered this year included cardiac regeneration, the role of inflammation and diabetes in heart disease, fetal heart development, cardiac remodelling, calcium signalling, and the role of epigenetics in the failing heart.

Our invited International Speakers this year were Prof Joseph Hill (UT Southwestern Medical Center), Dr Scot Matkovich (Washington University School of Medicine, JMCC sponsored guest) and Prof Litsa Kranias (University of Cincinnati). Prof Hill gave very informative lectures on future heart failure issues from emerging pre-diabetic populations. Dr Matkovich spoke on the role of noncoding miRNA and lncRNA in cardiac stress and disease, while Prof Kranias gave presentations on mutations in calcium cycling genes and the emerging role of HSP20 in cardiac function and survival. These lectures were complemented with presentations from our talented local scientists covering a broad spectrum of basic cardiac research that targeted physiology, pathology, cell signalling as well as genomic and transcriptomic mechanisms of healthy and diseased hearts. New in 2017 were JMCC-sponsored sessions on non-coding RNAs in health and disease.

The ISHR Australasian section has long been a proud supporter of both student and early postdoctoral researchers. Following on from the success of last year’s early career researcher (ECR) events, ISHR Australasian section ECR representatives Dr Helena Viola (University of Western Australia) and Dr Kimberley Mellor (University of Auckland), once again organised an outstanding Early Investigator Symposium and Panel Discussion. This pre-ISHR meeting event provides further opportunity for ECRs to engage with senior researchers, and present their work at a major conference. We had six outstanding presentations from ECRs revolving around the theme of molecular mechanisms and predictors of cardiac pathology. This year, for the very first time, several Early Career Investigator Oral Presentation prizes were made available, sponsored by ISHR-International. The presentations were of such outstanding quality that the judges could not split the winners. Joint first prize was awarded to Dr Kate Weeks and Dr Helena Qin (both from Baker Heart and Diabetes Institute), with a runner up prize being awarded to Ms Upasna Varma (University Melbourne). The symposium was followed by an informative Panel Discussion on ‘Gene manipulation in the future of cardiovascular therapeutics’ chaired by Dr Enzo Porrello (Murdoch Children’s Research Institute) and Prof Fadi Charchar (Federation University). To begin, Dr Jamie Vandenberg (Victor Chang Cardiac Research Institute) gave a basic mechanism perspective on this topic, while Dr Eddy Kizana (Westmead Institute for Medical Research) gave a clinical perspective. Following these talks, Dr Matkovich and Dr Adam Hill (Victor Chang Cardiac Research Institute) joined the discussion,
which included coverage of current knowledge of cardiac AAV gene therapy and the obstacles faced by researchers for the successful translation of cardiac AAV gene therapy into the clinic. Panel members and the audience provided engaging dialogue on this theme.

Further support for ECRs is reflected by the opportunities given to young researchers to present their work and compete for prizes. The 2017 ISHR Student Investigator Presentation Finalists were Ms My-Nhan Nguyen and Mr Darnel Prakoso (both from the Baker Heart and Diabetes Institute), Mr Mitchell Lock (University of South Australia) and Ms Choon Boon (Evangelyn Sim (University of Queensland). Well done to all of the students for their excellent presentations and responses to the questions from the audience. Congratulations to the winner, Ms Nguyen, for her presentation titled ‘Potential source of circulating galactin-3 in heart failure: studies on patients and cardiomyopathy mice’.

In addition to the ISHR Student Investigator presentations, the ISHR Mini Oral and Free Communication presentations are always popular, providing another avenue for discussion in cardiovascular research. These sessions were well attended and covered a wide range of topics from basic science, clinical, epidemiology, and studies conducted in mice, rats, sheep and humans. Congratulations to Mr Prakoso for winning Best Student Mini Oral for his presentation titled ‘Using gene delivery to target Cardiac O-GlcNAc protein modifications in the diabetic heart: Impact on left ventricular function’, and to Mr Matthew Chu (University of Adelaide) for the Best Free Communication presentation titled ‘Circulating secreted frizzled-related protein 5 (Sfrp5) is decreased in patients with diabetes and is associated with diabetic control’. Congratulations to all of the students who participated in these sessions.

The ISHR Student Publication Award was won by Mr Richard Tan (Heart Research Institute), for his paper entitled, ‘Non-invasive tracking of injected bone marrow mononuclear cells to injury and implanted biomaterials’ published in Acta Biomaterialia (2017, Volume 53, p378-388). In this paper, Richard demonstrated a new longitudinal tracking model that can non-invasively determine exogenous bone-marrow mononuclear cells homing and engraftment to biomaterials, providing a valuable tool to inform the design of scaffolds with implications for countless tissue engineering applications. Dr Francine Marques (Baker Heart and Diabetes Institute) took home the ISHR Postdoctoral Publication Award for her paper published in Circulation, titled ‘High-Fiber Diet and Acetate Supplementation Change the Gut Microbiota and Prevent the Development of Hypertension and Heart Failure in Hypertensive Mice’ (2017, Volume 135, p964-977). In this paper, Francine demonstrated that a diet high in fibre led to changes in the gut microbiota that played a protective role in the development of cardiovascular disease. The favourable effects of fibre may be explained by the generation and distribution of one of the main metabolites of the gut microbiota, the short-chain fatty acid acetate.

The ISHR Early Investigator Luncheon allowed delegates to interact with well-known international and local cardiac researchers and clinicians including Profs Hill, Kranias, Gemma Figtree (Univ of Sydney) and Dr Matkovich. This year’s format was extremely engaging as attendees were divided into smaller groups which allowed them to ask specific questions about career development to each panel member in a speed networking format. The overall concluding discussion covered topics including what each panellist would seek in potential post-doctoral candidates, advice on skills to increase competitiveness, and pursuing overseas post-doctoral positions. Special thanks to the organisers Drs Viola and Mellor who contribute their time to make this event, and the pre-ISHR meeting ECR events possible.

The annual AGM was held on Friday 11th August at the Novotel Langley Perth. Here Prof Livia Hool (President), Dr Colleen Thomas (Finance Secretary), A/Prof Rebecca Ritchie (Member Secretary), Dr Jim Bell and A/Prof Julie McMullen...
ISHR-ES/SERVIER FELLOWSHIP 2014

A ROLE FOR MICRORNA-423-5P IN ENDURANCE TRAINING-INDUCED SINUS BRADYCARDIA

It was a tremendous privilege to receive the 2014 ISHR-ES/SERVIER Research Fellowship at the ISHR European Section meeting in Barcelona. At the time, my postdoctoral work (with Professor Mark Boyett at the University of Manchester) had uncovered a role for electrophysiological remodelling of the hearts pacemaker, the sinus node, in the resting bradycardia of endurance exercise. The Award supported an investigation of underlying microRNA (miR)-based mechanisms controlling heart rate in the athlete and in the course of the Fellowship we identified a prominent role for miR-423-5p. Our work, summarised here, is the first exploration of ion channel remodelling in human endurance athletes and is the first demonstration of miR-dependent control of heart rate.

Heart rate is set by a relatively small population of myocytes in the sinoatrial node that possess a unique ion channel makeup and electrophysiological profile resulting in the generation of diastolic depolarisation and automaticity. Plasticity in the molecular profile of the sinus node allows for basal heart rate adaptation in response to acute and chronic stimuli. Modification of pacemaking ion channel expression is an important mechanism in heart rate regulation and has been reported in a range of physiological (e.g. ageing, athletic training) and pathological (e.g. heart failure, atrial fibrillation) settings resulting in changes to sinus node function. The upstream determinants of ion channel remodelling in the sinus node are not fully understood and here we focused on regulatory mechanisms controlling expression of the key pacemaking channel HCN4 in the context of endurance exercise.

Why do athletes have a slow heart rate?
There are well documented cardiac electrophysiological changes that accompany chronic vigorous endurance exercise, the most common of which is sinus bradycardia. Training-induced bradycardia is widely attributed to high vagal tone, but our recent work has stimulated debate on the relative contribution of altered autonomic nerve activity vs. intrinsic changes to sinus node pacemaking in underlying this effect. In two rodent models of exercise training, we demonstrated that training-induced bradycardia is predominantly the result of a downregulation of the key pacemaking ion channel HCN4 and its corresponding ionic current (funny current, $I_f$) in the sinus node. In the present study we first tested whether these concepts were applicable to human athletes. As shown in Fig. 1A, we demonstrated a lower intrinsic heart rate in endurance trained athletes vs. non athletes, recorded at baseline and on complete pharmacological block of the autonomic nervous system by application of previously validated doses of atropine and propranolol. This shows that resting bradycardia in human athletes cannot be attributed to heightened vagal tone. We then assessed the role of HCN remodelling in human athletes by administration of oral ivabradine that dose-dependently blocks HCN4 and $I_f$. Figure 1B demonstrates that athletic subjects (with a lower intrinsic heart rate after autonomic block) also had a blunted response to the heart rate-lowering effect of ivabradine, supporting a role for $I_f$ suppression in the trained human sinus node. To our knowledge this is the first (albeit indirect) evidence of pacemaker ion channel remodelling in human endurance athletes.

miR-423-5p controls HCN4 and $I_f$ in the trained sinus node
Having established a potential role for HCN4 remodelling in human athletes we went on to investigate an underlying role for miRs in a mouse model of swim training-induced bradycardia and HCN4 downregulation. Small non-coding RNAs including miRs are known to pay pivotal roles in controlling and fine tuning cardiac remodelling in physiological and pathological settings and previous work has shown that miRs regulate expression of ion channels in the heart. To investigate miR involvement in the training-induced downregulation of HCN4 we initially obtained an unbiased view of the ‘miRome’ in sinus node biopsies from bradycardic swim-trained mice and sedentary controls using (Illumina miSeq) next generation sequencing. In silico approaches were then applied to significantly dysregulated miRs (Fig. 2A) to generate a list of candidate miR-HCN4 pairs based on canonical complimentary base pairing between miRs and the HCN4 3’ untranslated region (UTR). These computational predictions were verified in vitro using a luciferase reporter gene assay wherein the HCN4 3’-UTR was fused to a lucif-
erase reporter gene and co-transfected with precursor miR-423 in h9c2 cells. Of the potential HCN4-targeting miRs tested, miR-423-5p produced the largest dose-dependent reduction in luciferase activity (Fig. 2B) and this effect was abolished by mutation of specific recognition elements in the HCN4 3’UTR (Fig. 2C). Interestingly, training-induced upregulation of miR-423-5p was restricted to the sinus node i.e. its expression was unaltered in the trained right atrium and left ventricle and was also restored on de-training (Fig 2D). These lines of evidence led to the hypothesis that the training-induced upregulation of miR-423-5p could trigger HCN4 downregulation and consequently a lower heart rate. We investigated this possibility further using a loss-of-function approach by in vivo administration of cholesterol-conjugated anti-miR-423-5p (antimiR). Remarkably, antimiR restored the heart rate measured in vivo and in vitro towards the pre-training level (Fig. 3A) concomitant with a reversal in protein levels of HCN4 (detected by western blot, Fig. 3B). Accordingly, whole cell patch clamp recordings from isolated sinus node cells confirmed a 54% percent reduction in \( I_f \) in trained mice that was almost fully restored in antimiR-treated trained mice (Figs. 3C and 3D). To our knowledge, these observations were the first report of miR-dependent control of pacemaking ion channels and heart rate.

**Concluding remarks**

In summary, research conducted during the ISHR-ES/Servier Fellowship confirmed the role of intrinsic changes to pacemaker electrophysiology in underlying the resting bradycardia of endurance exercise in human athletes and provided novel insight into training-induced epigenetic control mechanisms regulating heart rate.\(^{17}\) miRs have shown recent promise as ‘druggable’ targets approaching bedside transition\(^{18}\) and thus the finding of sinus node-specific up regulation of miR-423-5p as an important regulator of HCN4 expression might have translational potential, especially in...
the veteran (i.e. older) athlete; veteran athletes can present with a higher incidence of electronic pacemaker implantation for sinus node disease\textsuperscript{19-21} and targeting miRs in the sinus node may represent a viable alternative therapeutic strategy.

**References**


MEET THE 2017-2019 ISHR-NAS EARLY CAREER INVESTIGATOR (ECI) COMMITTEE

The ECI committee of the ISHR-NAS is dedicated to promoting training, development and networking among early career cardiovascular scientists - through organized events at ISHR Section Meetings as well as interactions over various digital platforms. We look forward to working with all members of the ISHR and are always seeking input from the community on how we can better serve you.

**Erik Blackwood** is a doctoral student in the Cell and Molecular Biology Joint Program at SDSU and UCSD in the lab of Dr. Chris Glembotski. Erik’s current research focuses on cardiac hormone secretion as a therapeutic target for hypertension and hypertrophic cardiomyopathy as well as drug development strategies for novel pharmacologic interventions in myocardial infarction or stroke.

**Samarjit (Sam) Das** is a Research Associate in the Cardiovascular Division of the Johns Hopkins School of Medicine. Sam’s research focuses on the functional consequences of microRNAs in cardiovascular disease. Sam’s lab is particularly interested in microRNAs which do not follow the conventional mRNA suppression pathway, mitochondrial microRNA biogenesis, and microRNA degradation pathways. They also study the phenomenon of cell-cell and organ-organ communication via exosomal microRNAs.

**Natasha Fillmore** is a postdoctoral fellow in the Laboratory of Cardiac Physiology with Dr. Elizabeth Murphy at the NHLBI, NIH. Natasha’s research interests include understanding the mechanisms involved in regulating energy metabolism and the development of cardiovascular disease.

**Manuel Rosa Garrido** is an Asst Project Scientist in the lab of Dr. Thomas Vondriska in the Department of Anesthesiology & Perioperative Medicine at UCLA. Manuel is focused on studying the structure of the cardiac genome during heart failure, in order to develop diagnostic features that can predict disease, greatly improve outcomes, and identify master regulators that can be manipulated therapeutically.

**Kim Ho** is a student in the Master of Science in Medical Sciences and Pediatrics program at the University of Alberta with Dr. Gary Lopaschuk and Dr. John Ussher. Kim is currently studying the cardiac metabolic perturbations that occur with heart failure and diabetes, specifically the mechanisms and implications of ketone body oxidation in these settings.

**Stephan Lange** is an Asst Professor in the Cardiovascular Division of the UC San Diego School of Medicine. Stephan’s lab investigates muscle development, signaling and maintenance, by studying the biological role of sarcomeric and muscle associated proteins. His group is particularly interested in deciphering molecular mechanisms that play a role in the development of cardiac and skeletal muscle myopathies, such as the signaling pathways driving dilated cardiomyopathy and the contribution of regulated protein turnover.

**Cat Makarewich** is a postdoctoral fellow in Dr. Eric Olson’s Lab in the Department of Molecular Biology at UT Southwestern Medical Center. Cat’s work has focused on a collection of small proteins encoded by short open reading frames hidden within RNAs that are incorrectly annotated as noncoding RNAs, specifically a subclass of these peptides that regulate contractility and calcium homeostasis in the heart. She is currently studying the function and regulation of these peptides during development and disease.

**Randi Parks** is a postdoctoral fellow with Dr. Elizabeth Murphy in the Laboratory of Cardiac Physiology, NHLBI, NIH. Randi’s overall research interest is in calcium signaling within subcellular compartments of the heart, both physiological and pathophysiological. Her current research is focused on understanding cardiac mitochondrial calcium flux and how calcium overload mediates mitochondria-triggered cell death via the permeability transition pore.
Ron Vagnozzi is a post-doctoral fellow with Dr. Jeff Molkentin in the Division of Molecular Cardiovascular Biology and the Heart Institute at Cincinnati Children’s Hospital. Ron is focused on mechanisms of tissue repair and injury resolution. He is currently exploring cellular processes underlying repair capacity in the adult heart, with an emphasis on macrophages and endothelial cells. His overall goal is to define endogenous mechanisms of the cardiac injury and stress response, and how these might be manipulated by new therapeutics.

We encourage everyone in the ISHR early career community to get involved! For more information please get in touch with us through the ISHR-NAS groups on Facebook: https://www.facebook.com/groups/ECI.ISHR/members/ or LinkedIn: https://www.linkedin.com/groups/2596502 and plan to join us on May 29 – June 1, 2018 for the ISHR-NAS Section Meeting in Halifax, which will feature an ECI scientific symposium and career development workshop!
members. In addition, Dr. Vila Petroff presented a report on ISHR-LA activities and announced the nominee for the President of the ISHR-LA 2018-2020, Sergio Lavandero. This proposal was approved unanimously, and after his first words as President-Elect we can confirm that the 2018 annual meeting will be in Santiago, Chile, and will surely be another successful event.

Our younger investigators and PhD students participated in two poster sessions in which they presented more than 30 posters with the latest unpublished data. These sessions were full of enthusiasm and covered all areas of cardiovascular research, creating the perfect opportunity for interaction between young and senior investigators. ISHR-LA also provided twenty travel awards for young fellows and investigators. The selected recipients were from Argentina, Chile and Brazil.

Many meeting participants took advantage of the opportunity to taste Mendoza’s wines complemented with typical Argentine beef in some of the many restaurants in the downtown area of Mendoza (a ‘must-do’ in this city) (Fig 2). Other attendees went horseback riding and sightseeing in the mountains. After the closing ceremony, the invited international speakers and the ISHR-LA committee were invited to a closing lunch at Bodega Séptima, one of the most important wine cellars in Mendoza and in the country (Fig 3). The participants promoted their mutual friendship with delicious food and one of the best red wines in Argentina in an intimate and friendly atmosphere. After lunch, they enjoyed a music band that encouraged all attendees to dance different rhythms, including Tango.

As mentioned previously, the next annual meeting (2018) will be held in Chile. We look forward to seeing each other again and sharing not only the latest developments in science from our region, but also our natural and true friendship. A special invitation is extended to all Sections of the ISHR. Finally, we want to thank ISHR-International for providing financial support for the two JMCC-sponsored symposia in the ISHR-LA 2017 Annual Meeting in Mendoza.

Carlos Valverde
Centro de Investigaciones Cardiovasculares “Dr Horacio E Cingolani”, Argentina
for Young Investigators was established in 1978 and 4 to 6 young investigators were invited to compete for the Award at each Congress. Likewise, the Council established the Peter Harris Distinguished Scientist Award and Outstanding Research Award in 1984 for the recognition of established investigators. The winners of both these Awards were carefully selected and invited to each Congress to give special lectures. All three Awards became very popular and lent respectability to ISHR.

It became increasingly difficult to fund the operation of ISHR with membership dues. Funding the organization of Congresses with donations from the pharmaceutical or medical device industries was difficult; furthermore, the services of a full-time individual was needed to run the affairs of ISHR. Thus funds from alternate resources were needed. Several individuals, including Drs Norman Alpert, Philip Poole-Wilson, David Hearse and Naranjan Dhalla, were successful in renegotiating the contract with Academic Press, London (JMCC Publisher) to provide substantial income to ISHR on an annual basis effective 1993. In addition, both Drs Howard Morgan (in his capacity as Chair of the ISHR Finance Committee) and Naranjan Dhalla (as President of ISHR) were successful in persuading Professor Makoto Nagano (President of the Japanese Section of ISHR) to obtain $300,000 for ISHR from his contacts in Japan. These funds were received in 1994 as endowments to hold 3 named symposia sessions at each ISHR Congress. The ISHR Council was authorized to select the speakers as well as topics for the Bayer, Canon and Koito Symposia and to use the interest from the Endowment Fund for expenses. Such efforts in fundraising and income generation built the financial base of the ISHR and offset operational costs.

Concluding Remarks
I have taken appropriate care in depicting events associated with numerous individuals, who in my opinion have served this organization in different capacities with great distinction. If I have made any omission or described any event inaccurately, it was not my intention to offend anybody because I have always believed that: "In this Mortal World, people come and go, they perform their tasks but do leave their footprints behind for others to trace the history for the development and progress of events, and particularly to appreciate the agony and ecstasy they experienced for the accomplishment of their mission". It is amazing to see that most of my professional life has revolved around this organization and its diverse members. I have served ISHR with a deep sense of commitment and extraordinary passion and I am grateful to the many cardiovascular leaders who gave me the opportunity to know them.

Naranjan S. Dhalla,
Distinguished Professor, University of Manitoba, Institute of Cardiovascular Sciences, Max Rady College of Medicine, St. Boniface Hospital Albrechtsen Research Centre, Winnipeg, Canada

1968 Founding Member of the Study Group/ISHR
1970 Council Member of the Study Group/ISHR
1972-1989 Secretary General of the Study Group/ISHR
1989-1998 Pres-Elect, President, Past-Pres of the ISHR

1974-1985 Exec Sec of the American Section
1985-1994 Pres-Elect, President, Past-Pres of the American Section

(ECR Development) gave a summary of the Australasian section’s activities over the past year. The AGM was followed by the annual ISHR dinner, also held at the Novotel Langley. The ISHR dinner made for a wonderful opportunity to network with fellow ISHR members and our international guests all while celebrating a highly successful meeting, the achievements of the section thus far, and stimulating lively discussion about the ever growing future of the Australasian section of the ISHR.

Mr Mitchell Lock, Mr Darnel Prakoso, Ms Choon Boon (Evangelyn) Sim and Dr Bianca Bernardo

The next CSANZ / ISHR Australasian Section meeting will be held in Queensland at the Brisbane Convention Centre, 2-5 August 2018.
HEART NEWS AND VIEWS

is the official News Bulletin of the International Society for Heart Research and is published every fourth month.

Editor
L. Anderson Lobaugh
Durham, NC, USA
E-mail llobaugh@nc.rr.com

Founding Editor
T.J.C. Ruigrok
Wijk bij Duurstede, The Netherlands
E-mail t.j.c.ruigrok@xs4all.nl

Editorial Board
R.A. Altschuld
Columbus, OH, USA
M. Avkiran
London, UK
Past-President
R. Bolli
Louisville, KY, USA
T. Izumi
Kanagawa, Japan
Japanese Section
B. Bernardo
Melbourne, Australia
Australasian Section
X.Y. Li
Beijing, China
Chinese Section
A. Mattiazzri
La Plata, Argentina
Latin American Section
B. McDermott
Belfast, UK
European Section
E. Murphy
Bethesda, MD, USA
President
T. Ravingerova
Bratislava, Slovak Republic
A.-M.L. Seymour
Hull, UK
N. Takeda
Tokyo, Japan
K.K. Talwar
Chandigarh, India
Indian Section
D. Eisner
Manchester, UK
B.J. Ward
London, UK
K.T. Weber
Memphis, TN, USA

Editorial Office
3711 Lochn’ora Parkway
Durham, NC 27705
USA.
Phone/Fax: +1 919 493 4418

DIALOGUES IN CARDIOVASCULAR MEDICINE

Get the latest news from the main cardiology meetings!
The journal provides up-to-date information on specific areas of cardiovascular medicine and encourages dialogue between key opinion leaders and readers.

Read the latest issue online:
www.dialogues-cvm.com

OCTOBER 2017
VOLUME 22
#3

2017
ESC
Barcelona
www.dialogues-cvm.com

This publication is supported by an unrestricted grant from Institut La Conférence Hippocrate - Servier Research Group

ESC
Barcelona
2017