As a practicing cardiologist, and as one of Professor Krebs’s last graduate students, I recently read a portrait by Dr. Mark Nicholls in the European Heart Journal (1). I read it with personal interest. While the accounts are accurate (and well presented), the author probably has never met Hans Krebs. Until late in his life, Krebs also had no particular interest in the heart. Therefore, I would like to share some personal recollections from my time in the Krebs lab (1978-1981).

I have fond memories of the Metabolic Research Laboratory in Oxford, mostly because of Krebs’ infectious enthusiasm for science, and, because of a congenial group of coworkers. They came both from Britain, and from all over the world. In the lab, we called our leader simply the “Prof.”. Krebs was an unassuming person of extraordinary discipline, a superior mind, well deserving his nickname. No one would argue with him.

**Finding my way to the Krebs Lab:**

I am sometimes asked: “How did you end up in the Krebs lab?” I am still struggling to find the right answer. Like every medical student, I had once memorized the Krebs cycle. I was attracted by its logic, and on a personal note, I knew that Krebs had come to England from Germany. During my cardiology fellowship at the Brigham in Boston, I got hooked on cardiac metabolism through my mentor, Dr. Michael Lesch. Perhaps it was my ambition to excel that I contacted Krebs when I read an article about...
his lab in Oxford. Admittedly, I took the first step by writing to Krebs with a proposal to study branched-chain amino acid metabolism in isolated heart muscle cells. Krebs would not have any of it, and he showed little interest at first.

**Krebs and the heart**: In fact, throughout his career, Krebs had avoided to study metabolism of the heart or the brain (Brian Ross, personal communication). Even Lionel Opie, one of the fathers of cardiac metabolism and a Rhodes Scholar in the Krebs lab in the late 50s, was not able to write a paper with Krebs. However, in 1970 Krebs had agreed to serve as one of the founding editors of the *Journal of Molecular and Cellular Cardiology*, together with Lionel Opie and Richard Bing. The whole initiative of starting a new journal I find amazing because 50 years ago, cardiology was dominated by hemodynamics and imaging. Indeed, very few people thought in terms like “molecular” and “cellular” cardiology. Krebs supported the cause, I think, simply by lending his name to the new adventure. As an aside, Krebs was eager to read manuscripts. When he reviewed manuscripts, he taught me how to be detailed, constructive, and decisive.

Continuing with my story, Krebs took the second step a few weeks later, by interviewing me during a layover between two flights at Logan Airport in Boston. Things happened rather quickly thereafter. Another few weeks on, my family and I were in Oxford—myself with instructions to develop my own experimental tools under the guidance of Reg Hems (about whom I will talk later). Looking back, I shudder at taking such a great risk without thinking of the consequences. All came to a good end, though, and I credit the support of Reg Hems (about whom I will talk later), who was as ever discarded. Envelopes were slit open and served as scrap paper, sometimes to capture an elusive thought, and always to write down the day’s “to-do” list. The Prof. set the example.

It may sound trivial, but such habits may have contributed to the Prof.’s profound insights into the fundamental processes of life. Waste not, want not. This is what he said at the end of his Nobel Lecture in 1953: *The concept of evolution postulates that living organisms have common roots, and in turn the existence of common features is powerful support for the concept of evolution. The presence of the same mechanism of energy production in all forms of life suggests two other inferences, firstly, that the mechanism of energy production has arisen very early in the evolutionary process, and secondly, that life, in its present forms, has arisen only once* (6).

**Unity in diversity**: The Metabolic Research Laboratory never had more than a dozen members, but they were an ideal mix of both senior and junior investigators, working on about half a dozen (or more) distinctly different projects at a time. A special feature of the lab were its collaborators or “honorary members”. Prominent among them was Frederic (Larry) Holmes, professor for the History of Science at Yale University, traveling to Oxford regularly to interview the Prof. and to review material for Krebs’ masterful biography (7).

It was Krebs’ quiet influence that during the week the lab was literally “humming” in the same rhythm, with a coffee break at 11:00 am and a tea break at 3:00 pm. Attendance was expected, but not mandatory. In hindsight, I realize that both breaks amounted to two short informal lab meetings every day. Back then, it was sometimes a challenge for me to fit in the protocols for my working heart perfusions (8) into this schedule. But the main effect on all of us was the same: Someone cared (Fig. 1).

Our meetings were held in the lab’s library, one flight of stairs above the lab. Krebs was of relatively small stature, but, even in his
late 70s, he always took two stairs at a time while going upstairs, wasting no time. There are many anecdotes about Krebs being parsimonious with both time and resources, as already mentioned. More importantly, Krebs often referred to his “time to think” when he was washing the glassware for his own experiments, or when he was meticulously tending to his large garden in Abberbury Road. As an aside, Krebs also mentioned to me once that lying awake at night did not trouble him. It was “time to think” for him as well. When we asked him once what he was thinking about, he quoted Albert Einstein: “Oh, I have many good thoughts. But at the end of the day, most of them are useless.”

Krebs - a workaholic?: Like many great minds, Krebs had also his detractors. Some of those called the Prof. a “workaholic”. However, this is far from the truth for those who knew him well. Admittedly, he expected us to be in the lab on Saturdays from 8 until noon, but the lab was closed every weekday at 6:00 pm. No one was allowed to work in the lab alone! The Prof. was also fond of the phrase: “Get some rest”. Equally important, like it is the custom in England, a three week summer holiday was a well-guarded privilege (and strongly encouraged by the Prof.). My wife turned this into an adventure for our young family when we rented a cottage in Tresco, an island of the Isles of Scilly in Cornwall. It still pains me, though, in hindsight that I spoiled part of our last summer holiday on Tresco by reading Lehninger’s textbook of Biochemistry. Rumor had it that “anything in Lehninger will be fair game” in the viva (PhD defense).

Back to Krebs. Part of his success was his discipline, including playing the piano for 15 minutes every night before retiring (G. Saez, personal communication). As already mentioned, Krebs also tended to a most interesting garden, indeed we thought of him as a botanist at heart. He knew each and every plant in his garden by its English, German and Latin name. “Everything in nature has a name”, he told our children on a walk through his garden. Amazing, but an understandable teaching point to those who knew him well. Admittedly, he was washing the glassware for his own experiments, or when he was be it in front of the spectrometer, or be it within the lab. A further recollection regarding visitors were the brilliant seminars given to the lab by some of them. “The Americans always carry a set of slides with them, prepared to give a seminar”, the Prof. liked to say with a smile. He was known (and loved) for his impish sense of humor. All this means that in the lab, we were the beneficiaries of a vibrant research environment. The environment was further enriched by individuals like Herman (Hugh) Blaschko, a retired Oxford Pharmacologist and the Prof.’s life-long friend, and by Eric Newsholme who drew crowds of students (including me) to his lectures on regulation of metabolism in the main amphitheater of the Biochemistry Department across the street from the Metabolic Research Lab.

A Perfect Infrastructure: Krebs was surrounded by a team, he referred to as the “senior members” of the lab, Dermot Hedley (Derek) Williamson, Patricia (Pat) Lund, Reginald (Reg) Hems, David (Dave) Wiggins, and Marion Stubbs (who worked part-time while raising her family). I fondly remember each one of them and the other members of the lab. It would take another article to do justice to them all. Very briefly, Derek was world-renowned for his work on ketone body metabolism and the metabolism of mammary gland cells. Pat was widely known for her work on glutamine metabolism and colonocytes (both hot topics today in cancer cell metabolism), and Marion was world-renowned for her work on the control of the redox state. Marion was also one of many unsung heroes of the lab because she isolated (for me and others) an enzyme that we used extensively for some of my assays. Her isolations, though, started for me with a trip to the abattoir in Thame, a market town outside Oxford, to collect a pig heart at 4:30 in the morning.

At peak times, there were 15 of us, including the Prof. who had his desk in the lab. Another amusing story comes to mind: The lab had only one telephone, which was mounted on the wall next to the main entrance door. Whenever the phone rang, the one who happened to be closest to it, picked it up by saying “Extension 311”, and then shouted out the name of the person the call was for: “Prof.”, “Pat”, or “Derek”, etc. I would not tell this story, had it not been for the fact that a large volume of the incoming calls were directed at Derek. He was the editor of the Biochemical Journal at the time! Authors were ringing throughout the day, and they were ringing from all over the world. There was an unwritten rule for all of us: What was heard in the lab, stayed in the lab. Mind you, those were also the days before wordprocessors and before the internet.

Lastly, I observed that the Prof. would rarely make a decision regarding the lab without consulting the senior members of the
Continuing a habit he had learned during his medical training, Krebs would “go on rounds”, visiting every one of us at the bench, every morning. Conversations could easily be overheard so he did indeed consult with us. In the case of a student, like me, he was almost fanatic about reviewing notebook entries; in the case of the senior members (who ran their own projects), the discussions centered more on results and strategies. It all sounds quite strict, but the spirit of the lab was always positive and uplifting. Even though it was painful to admit mistakes, it did not keep us from trying, and trying again.

An Ode to Reg Hems: Among the senior members, the one assigned to me was Reg Hems (Fig. 2), who served as my immediate supervisor and co-supervisor for my thesis. It was Reg who introduced me to the real world of metabolism and who did not shy away from taking a “mature” graduate student under his wings (at the time I joined the lab, I was already 37 years old and also already a board-certified cardiologist). Reg and I had our desks side-by-side, squeezed at the end of an aisle between two long lab benches. Reg introduced me to about everyone I needed to know in the Oxford Science Area, from the glassblower to the machine shop, from the cryo-lab in the Physics Department to the lab in the Organic Chemistry Department where Professor Baldwin’s group made artificial hemoglobin (which I then tested in my heart perfusions). I followed Reg like a puppy. More than that, Reg taught me everything I needed to master at the bench.

What I liked perhaps the most about Reg was his attitude to problem-solving. “Getting stuck” (a phrase the Prof. used quite often!) seemed often a welcome challenge for Reg. That’s why I went first to Reg for advice with my benchwork. He used the same rational approach over and over again: “Let’s sit down and think for a moment”. Reg had a wonderful way to make me (and everyone else) feel at ease. Next: “Tell me what you did / or what you observed, tell me from the very beginning, and then let’s move on step-by-step. Let’s look at your notebook, let’s repeat the experiment together if necessary”. Most of the time we were able to solve the issue. Reg’s experience at the bench also showed through when he joked how an experiment works perfectly well the first time around, but then not the second, and not the third time around. “Stay with it” were his favorite three words. Every time I use these words in my own lab, I think of Reg, even today. Another phrase Reg liked to use in his role as lab manager when our demands became too much, was “I am surrounded by idiots” – which caused me to cringe because my desk was right next to his.

Much more remarkable is Reg’s career path in research. He became an independent investigator (and the friend of many other investigators) without a formal academic degree. It was only towards the end of Reg’s active career in research that the University of Oxford awarded him a Master of Arts (MA) degree, and that was by necessity (it was required so he could be my co-supervisor). I know how difficult it was for Reg personally at the time to accept this degree. Reg called himself first a “Yorkshire lad” and was very proud of it. He was born and raised in Sheffield, and joined Krebs lab at the University of Sheffield as a “lab boy” when he left school at the age of 14. Reg never had another job; he moved with Krebs to Oxford in 1957, and ran the “Unit of Metabolic Research” at the Biochemistry Department, and later (after Prof’s official “retirement”) at the Nuffield Department of Clinical Medicine in the Radcliffe Infirmary on Woodstock Road— the storied Metabolic Research Laboratory. Besides running the lab and teaching students (me being one of them) at the bench, Reg also attended to his own research program. In more than 60 original papers he unraveled mechanisms of ketogenesis, de novo lipogenesis, and glutathione metabolism in the liver and isolated hepatocytes. What I find most interesting, Reg discovered the mitochondrial compartmentation of metabolic CO₂ (9) (10). Reg’s last paper was, however, a personal reflection entitled “How I became a biochemist” (11). It tells us that it is not the degrees but the love of the subject, and that it is also the good fortune of being at the right place at the right time. Perhaps the highest recognition for his dedication to the lab was that Reg was awarded an OBE (Order of the British Empire) in 1985 for Services to Biochemistry. Reg Hems’ picture is the only picture (Fig. 2) hanging on my wall in the office here in Houston. He greets me every day on coming to work.

Writing a Manuscript with the Prof.: Writing a manuscript with Prof. was an experience to behold. First, “If a biological problem were easy to solve, someone before you would have already done it”, Krebs used to tell me. Say it upfront why you did the work and what you found that’s new. Secondly, he insisted on both accuracy

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**Fig 2: Reginal Hems OBE (1922-2009), next to the oxygenator he designed for optimal organ perfusions.**
and brevity. How can this be accomplished? Krebs quietly put the typed version of a poem and put it on my desk (12) while I was writing my thesis. It begins as follows:

If you’ve got a thought that’s happy –  
Boil it down.
Make it short, and crisp and snappy –  
Boil it down.
If you want your effort printed….  
Boil it down.

Further linguistic training from the Prof included pointing out the beauty and precision of English. English, he said, contains far more words than German. Also, according to the Prof: Shakespeare has been fully incorporated into the fabric of German culture, mainly due to the competent translation of his works by Johann Schlegel (1719-49). Conversely, according to Krebs, there is no competent translation of Goethe’s “Faust” from German into English. One of Prof.’s “teaching moments” while we were writing on the Methods section of a manuscript! By editing my writing in small installments, he instilled in me enormous respect for the English language. At one time, I remember, he referred me to the story of Roget’s Thesaurus. Dr.Roget was a French physician who came to England during the French revolution. Dr. Roget taught himself English by listening carefully and listing all the synonyms for new words he had learned. Today, I still prefer Roget’s Thesaurus over any computer-generated synonym finder – because “it teaches you something”, as Krebs liked to say.

Making room for the new: I remember Krebs as a man always on the go. In 1978, the Prof decided to get rid of some clutter in the lab’s small library. He put up a bin into which he threw his old reprints. “All superseded” he grumbled, “we need to make room for new work”. I helped myself generously, rummaging through the discarded papers, found a reprint of Nobel Prize lecture in 1953, and asked him to sign it – which he did, with a faint smile on his face (Fig. 3). Keeping up with the research literature required some ingenuity before the introduction of the internet. The MRL subscribed to the BJ (Biochemical Journal) and the JBC (Journal of Biological Chemistry) to Science and, to Nature. In addition to the library upstairs, bound volumes of the journals were also kept in the lab itself. Later I learned that the Prof was a bibliophile (G. Saez, personal communication). In practical terms, Derek had taken on the role of the lab’s “scout”. Once a week, he went through the Science Citation Index, typed out all new papers of potential interest, and distributed carbon copies to each member of the lab. An incredible service to the lab aided by Marg Barber, the lab’s secretary, and Vera Ilic, Derek’s trusted research assistant.

A Student’s Family Life: I would be remiss not to mention that all these wonderful recollections could not be written without giving the greatest credit to my wife, and our three children who were 6, 8, and 12 years old when their father decided to uproot the family once more, seven years after we had come from Germany to Boston in Massachusetts. Moving from Boston to Oxford was one adventure, but moving within Oxford was another. While the lab stayed always the same, we had to move many times as a family while I was a graduate student. Housing for visitors in Oxford was very tight. Today we often ask ourselves, how we managed at the time. But manage we did, often through the kindness of strangers. And we became anglophiles. Two of our children are firmly rooted in Britain, and all three of them live and work in Europe.

Closing out: Krebs was a modest, gentle, and rational person. He asked me once: Did you not learn in school “suaviter in modo, fortiter in re” (Latin for “pleasantly in manner, powerfully in the cause”)? Although physically fit to the end of his life, Krebs must have been very much aware of his life cycle, and he acted accordingly. For instance, he met with a writer for two hours every morning, to whom he dictated the chapters of his life. He had done the same already before, writing the life story of his teacher, Otto Warburg (13). I witnessed how Krebs himself, saw the publication of his own autobiography “Reminiscences and Reflections (4) not long before he died in 1981.

I would like to close with one more anecdote. In 1980, when we asked Krebs what he had planned for his 80th birthday, he did not hesitate to answer: “Come to work as usual”. No wonder then, that Krebs’s last words to me were: “Heinrich, do you have any new results?”. And the beat continues for some of us still today. Lastly, I must mention that after the Prof. had died, it was Lady Krebs, as
When I wrote my last President’s Letter in May 2020, I did not imagine that now, 11 months later, we would still be in the midst of the Covid-19 crisis. I was worried, as all of us were, at a time when we had approximately 600,000 new cases per week, which seemed already astronomical. Since that time, numbers increased to more than 5,000,000 new cases per week in January 2021 and are still at approximately 2,000,000 per week. Almost 3,000,000 people lost their life due to this virus, increasingly also younger ones. And the mortality rate is now globally more than 2/100. What a crisis!

But it is not only the direct consequences of illness which threatens all of us. We face restrictions of personal freedom that are unprecedented and will leave a mark on each of us. I feel that, in the meantime, most of us adopted a somewhat fatalistic approach to the lack of freedom to travel, to elaborate any kind of cultural life, to meet friends and family and/or to simply go shopping. We got used to wearing masks, disinfecting hands before and after shopping and greeting others from a distance or by elbow-check, and still we seem far away from being in control of the pandemic. A year ago, we expected the partial shutdown to last for a few months, maybe a year, but now two years seems a much more realistic if not optimistic view. What this means for the global economy is completely unpredictable, but evidently the pandemic hits the underprivileged significantly harder than the wealthy. And this is true not only when comparing countries, but also when comparing different parts of the society in a given country. Not a new conclusion, but a crisis always hits the poorest and increases the economic gap in a society.

While the mortality risk is much higher for the elderly, the indirect damage seems to particularly hit the younger generation. I sometimes try to imagine what I would have done as a pupil being restricted in my learning to a PC and online teaching. Would I have concentrated on it or would I rather have taken a book and gone out into the forest, listened to music or played with my siblings? And what about the great time I had during my university studies? This was so much more than learning anatomy or biochemistry. It was, to a large extent, about meeting new people, making friends for life, finding a partner, experiencing new things and developing social skills. All of this is impossible at present. I hope that these opportunities come back soon and rely on the resilience of the young to make up for lost time.

And what about our scientific life? Of course, we are all experienced users of video conference tools, give “live” talks and record presentations to keep the ball rolling. By communicating virtually, we save travel time, are less jet-lagged and pollute the planet less. But I have to admit that the impact of virtual conferences is far less than that of real meetings. When I travelled to conferences in the past, my concentration on the subject began in the plane or train and carried on throughout the conference. I was far away from the duties of my work and life at home, so I concentrated on the conference, participated in talks even if they were not directly in my field of research, learned a lot and contributed to the discussion. And in the evening, I met with colleagues and friends, discussed the conference and life in general and built a network. All of this is missing in virtual conferences. I sit in my office or at home with lots of things around to do and deadlines waiting, and the camera and microphone are easy to close. So I give my talk, receive, in general, very few questions, and continue my usual work. In the evening of such a day, the conference has left almost no trace. Maybe others are doing better, but I hear many colleagues relate similar experiences. So even if virtual meetings replace many business meetings in the post-Covid future, I am looking forward to returning to old habits at least for the truly scientific meetings.

These considerations apply to our recent ISHR meetings. All ISHR section meetings had to be postponed or cancelled in 2020, with the hope that 2021 would see a return to normal. Unfortunately, that’s not the case. We will very likely have no in-person ISHR section
Dear colleagues,

It is my great honor and pleasure to host the XXIV World Congress of the International Society of Heart Research on 12–15 June 2022 in Berlin. The preparation for the congress is going well, and registration will open soon. As the president of the world congress, I proudly invite you to Berlin, one of the most vibrant cities in Europe. The scientific program committee is putting together an exciting program, and we promise you four days of cutting edge science and interactions. The congress will take place within the heart of the city, allowing efficient use of spare time for visiting Berlin. You are cordially invited to join and share in the excitement and success of the 2022 World Congress in Berlin.

Prof. Dr. Burkert Pieske
President, the ISHR XXIV World Congress
Director, Department of Internal Medicine and Cardiology, Campus Virchow-Klinikum Charité
Universitätsmedizin Berlin, Germany and German Heart Center, Berlin, Germany

www.ishr2022berlin.de
REPORT ON THE XV CHINESE SECTION MEETING  
(OCTOBER 18-20, 2020; BEIJING, CHINA) 

The 15th Annual Meeting of the International Society for Heart Research (ISHR) - Chinese Section (ISHR-CHI) was organized jointly with the Cardiovascular Society of Chinese Association of Pathophysiology (CAP) with the support of the Key Laboratory of Molecular Cardiovascular Sciences, Ministry of Education. The conference started with a Welcome and Opening Ceremony at the Beiyuan Grand Hotel South Lecture Hall on Oct 18th, 2020. The meeting was a combination of live and online sessions hosted by the current Secretary of ISHR-CHI, Prof XU Ming. Over one hundred representatives from ISHR-CHI and the Cardiovascular Society of CAP were invited to the live Opening Ceremony, with thousands of delegates attending online. The joint Conference Chairmen, Prof YU Xiyong and Prof ZHANG Youyi, delivered short welcome speeches. ISHR-CHI also conducted Section elections; the new leadership team was nominated and elected by current committee members by anonymous vote.

Publishing with the Journal of Molecular and Cellular Cardiology (JMCC)

A session for communication with the Journal of Molecular and Cellular Cardiology (JMCC) editorial team was arranged before the keynote speeches. Representatives from the editorial team of JMCC announced their new team and several new initiatives for the coming year. They also discussed new requirements and made suggestions to the on-site and online Chinese authors regarding some new features of JMCC.

Dr. Koos Admiraal, Senior Publisher, Elsevier Science Publishing, provided a video overview of JMCC. JMCC is a high-standard journal for publishing cardiovascular research (80% rejection rate) which has significant influence in the field. Several highly-cited articles have been published in the journal during the last few years, particularly in special issues. Co-chair of the session, Prof YANG Huangtian, Associate Editor, JMCC, offered advice to Chinese authors. She mentioned that while China is the top country for submitting articles to JMCC, the accepted rate is much less than that of US authors. Dr. Yang explained the reasons and provided some suggestions to Chinese authors interested in submitting papers to JMCC. In a video presentation, Prof. Michael Regnier, Deputy Editor of JMCC, introduced some of the new initiatives adopted by the journal. JMCC installed a new editorial board last year headed by Editor in Chief, Dr. TIAN Rong, and many new initiatives have been launched since that time. First, a new cover page for the journal has been designed and applied. In addition, the author guidelines have been modified, adding new article categories, new research areas for authors and new submission requirements. A new official website and social media platforms have been launched to make JMCC a more popular and global journal. Several special issues are now in preparation: one special issue on COVID-19 has accepted 14 articles out of 35 submissions. Editor’s Choice articles, a junior reviewer program and good reviewer incentive programs have been started to promote article quality. Prof Rong TIAN also discussed the impact of JMCC in an online presentation. Prof
TIAN answered questions together with Dr. Regnier and Prof. Yang, who was on-site with the audience, mostly concerning the modified areas of interest, design of the special issues and details of the reviewer incentive program.

Keynote Speeches

Speech 1: Dilated Cardiomyopathy and Macrophage
Presenter: CHEN Qi, Nanjing Medical University

Prof. Chen shared his recent work about dilated cardiomyopathy and macrophage published in Circulation Research. Doxorubicin-induced cardiomyopathy (DiCM) is a primary cause of heart failure and mortality in cancer patients, in which macrophage-orchestrated inflammation serves as an essential pathological mechanism. They found in DiCM, monocyte-derived macrophages primarily exhibited a pro-inflammatory phenotype that dominated the whole DiCM pathological process and impaired cardiac function. In contrast, cardiac resident macrophages were vulnerable to doxorubicin insult. The surviving resident macrophages exhibited enhanced proliferation and conferred a reparative role. Global or myeloid specifically ablation of SR-A1 inhibited proliferation of cardiac resident reparative macrophage proliferation.

Speech 2: Mitochondrial damage and metabolic cardiomyopathy
Presenter: REN Jun, Zhongshan Hospital of Fudan University

Prof. Ren summarized the work of his research team and recent developments regarding mitochondrial damage and metabolic cardiomyopathy. Prof Ren summed up the recent findings on the pathophysiological role of dysregulated autophagy which confers cardiac mitochondrial damage and development of metabolic cardiomyopathy. Finally, he suggested that targeting mitochondrial dysregulation through autophagy may become a novel therapeutic target for metabolic cardiomyopathy.

Speech 3: Prostaglandin D2 and pulmonary vascular remodeling
Presenter: YU Ying, Tianjin Medical University

Prof. Yu shared with the audience his work on prostaglandin and pulmonary vascular remodeling. Pulmonary arterial hypertension (PAH) is a life-threatening disease characterized by progressive pulmonary vessel remodeling. Prostaglandins (PGs) are responsible for the phenotypic transformation of pulmonary artery endothelial cells during PAH. Niacin has been reported to induce cutaneous vasodilation (facial flushing), which is mediated by enhanced PGD2 production. They found that niacin blocked the progression of PH induced by both hypoxia and SU5416 in rodents through a reduction of vascular remodeling achieved by stimulating H-PGDS-dependent PGD2 release from macrophages. Thus, niacin may serve as a therapeutic option for PAH.

Parallel Sections

In the afternoon, 3 parallel discussion forums were held, including the Heart Forum, Vascular Forum and ECI Forum. In the Heart Forum, 6 researchers shared their findings and views on heart disease involving inflammation, myocardial mechanical properties, mitochondrial damage, cardiac matrix stiffness and other potential therapeutic targets. In the Vascular Forum, 5 researchers presented their work about vascular diseases related to chemokine receptor-regulated macrophage, protein sulfhydryl modification, molecular imaging, circadian rhythm and CSE/H2-involved immune-inflammatory mechanism. In the ECI Forum, 11 young investigators shared their latest cardiovascular research. Their topics covered a broad spectrum of research interests for finding a cure for heart disease. There was a lively exchange of views between the presenters and the on-site audience.

Closing Ceremony

The closing ceremony of the joint conference, chaired by Prof. XU Ming, the past Secretary of ISHR-CHI, was held after the research sessions. Hundreds of on-site attendees, keynote and specialized report participants, young investigators and students benefited in many ways from this conference. Moreover, over 9000 online...
delegates attended the keynote speeches, and the two parallel sections were viewed online by up to 6000 and 4000 people, respectively. Prof. Xu announced the list of the new committee members and leadership-team; 73 committee members and 25 members of a young-investigator committee for ISHR-CHI were elected. A certificate was issued to each member of the new leadership-team by former members. In his closing remarks for the joint conference, the President of ISHR-CHI, Prof ZHU Yi, successfully concluded our meeting in Beijing, encouraged more participation and contributions from Chinese cardiovascular researchers and invited us to look forward to the next ISHR World Congress in Berlin in 2022.

Junjie Xiao
Shanghai University

8th Leadership committee of ISHR
Chinese Section:
Honorary Chairman:
HAN Qide
Honorary Co-Chairman:
ZHANG Youyi
Chairman: ZHU Yi

Vice Chairman: YANG Huangtian, DONG Erdan, HUANG Yu, WANG Daowen, XU Ming
Secretary: XIAO Junjie
Deputy Secretary:
XIAO Han, SHEN Ao
Treasurer: LI Li

8th ECI committee of ISHR
Chinese Section:
Chairman: ZHANG Li
Deputy Chairman: GONG Kaizheng, AI Ding, ZHANG Yingmei

2022 Fellows of the ISHR – Call for Nominations

The ISHR invites you to nominate candidates to be considered for appointment as Fellows of the ISHR (FISHR).

Fellowship status recognizes those members who have distinguished themselves for outstanding contributions to cardiovascular research. Fellows are appointed every 3 years, at the time of each World Congress. Nominees must be ISHR members in good standing for at least one year immediately preceding their nomination. Detailed guidelines and a list of current Fellows are available on the ISHR website (https://ishrworld.org). Please submit the name(s) and institute(s) of your nominee(s) along with a one-page nomination letter to the Executive Secretary (llobaugh@ishrworld.org) by July 1, 2021.
DAVID A. KASS, M.D.
LEVERAGING PROTEIN KINASE G TO TREAT HEART DISEASE
WINNER OF THE 2018 PETER HARRIS DISTINGUISHED SCIENTIST AWARD
(AUGUST, 2018; BRISBANE, AUSTRALIA)

David Kass is the Abraham and Virginia Weiss Professor of Cardiology, Professor of Medicine, Pharmacology and Molecular Sciences, and Biomedical Engineering at the Johns Hopkins University. He received his BA from Harvard College in 1975, where he majored in Applied Physics and Engineering, and in 1980, a Doctor of Medicine degree from Yale University. After completing residency in Internal Medicine at George Washington University, in Washington DC, he joined the Johns Hopkins Cardiology Division first as a fellow in 1983, and on faculty in 1986; he has remained there since. In addition to his academic appointments, David directs the Institute of CardioScience, and co-directs a decades long post-doctoral NIH-training program in Cardiovascular Disease. Among his honors are the Melvin Marcus Award (1st one), George Brown Lectureship, and Basic Science Award from the American Heart Association, and has served as Associate Editor for Circulation Research, and currently for American Journal of Physiology, and is editorial boards of Circulation and Circulation Research. David’s work spans from basic molecular and cellular research through to human studies. Many fields can claim a landmark study of his that played a key role and forged a new and important direction for research. All told, David has published over 500 original papers, garnering >47,000 citations with a Scopus H-index of 115; (Google Scholar 140). He has directly mentored over 100 students in his laboratory, and many are current academic leaders in cardiovascular research and/or medicine.

David caught a serious case of the research bug while in college working in the laboratory of Martin Moore-Ede, a circadian rhythm biologist in Harvard’s Physiology Department. Here, he melded his applied mathematics interests with biology to study bio-oscillatory behavior. As a Yale medical student, he was required to write a “thesis” and for this, he returned to the Moore-Ede lab, ultimately taking a year off to pursue the work. During this period, he uncovered how the Henry Gauer reflex (central volume receptor regulation – before atrial natriuretic peptide was discovered) was under potent circadian control. The work received an Annual Award from the Renal Section of the APS, and he knew he’d be a Physician Scientist after that. During residency, he was intrigued with the rapid advances being made in Cardiology and role bioengineering was playing. Once at Johns Hopkins, he joined the laboratory of Kiichi Sagawa, who in the late 1970’s had re-invigorated cardiac mechanics thought his landmark work on pressure-volume relationships. David’s first project translated this approach in vivo, using a newly developed catheter. He soon was using it in patients, and before completing fellowship, became the world’s first to implement PV analysis to dissect disease pathophysiology in intact humans. For nearly 15 years thereafter, he used systems physiology and bio-engineering to study intact heart and coronary mechanics, ventricular-arterial interactions, and determine how the heart is disabled by disease and ways to fix it. Highlights of his early studies were the impact of external constraints on diastolic properties, ventricular-vascular stiffening with aging and influence on cardiac mechano-energetics, and pulse-perfusion mechanics and endothelial-mechanosensing. In the late 1990’s he pioneered human studies of a pacemaker therapy known as cardiac resynchronization (CRT), used to treat patients with heart failure and conduction delay causing dyssynchronous contraction. This became the first new...
A memorable 2020
2020 brought a host of new initiatives to JMCC. One of our most timely efforts was the call for COVID-19 papers. We are proud to have published some outstanding research to share insights into the cardiac implications for COVID. Our task force of editors managed submissions quickly and ultimately published 17 throughout the year. We hope you have had a chance to read this important work, including one of JMCC’s top downloaded papers of 2020, “SARS-CoV-2 receptor ACE2-dependent implications on the cardiovascular system: From basic science to clinical implications.” (J Mol Cell Cardiol. 2020 Jul;144:47-53. doi: 10.1016/j.yjmcc.2020.04.031).

We launched several special issues on topics of interest to our readership. Our team’s first Special Issue, Unsolved Mysteries and Controversies of Mitochondria in the Heart, is now complete. Guest Editors Shey-Shing Sheu and Wang Wang gathered an extraordinary collection of papers presenting all sides of controversial topics related to mitochondria. We appreciate their hard work and hope that you check out the special issue at https://www.jmmc-online.com/content/unsolvedmysteries.

We also published the first papers in Special Issues on Cutting Edge Technology in Cardiovascular Research, edited by Rebekah Gundry and Kenneth Boheler; Cardiac Epigenetics: Driving signals to the cardiac epigenome in development and disease, edited by Emma Robinson, Manuel Rosa-Garrido, Chukwumeka George Anene-Nzelu, and Roger Foo. Three new special issues on Computational Models of Cardiovascular Regulatory Mechanisms; An Engineers Guide To Unlocking The Secrets Of The Cardiac Microenvironment; and Cardio-Oncology: Novel Molecular Mechanisms and Innovative Approaches will launch in 2021.

In February, we began naming “Editor’s Choice” papers each month to bring greater attention to the novel research in JMCC and to highlight the authors of this work. Editor’s Choice selections are free to read, to make this outstanding research accessible to everyone. You can find all of our 2020 selections on our website at jmcc-online.com.

New plans for 2021
Even more new initiatives are in the works for 2021. One of our big goals in our first year was to help JMCC reach a wider audience. In 2020 we launched new social media accounts (follow us at @jmcccardiology on Twitter and Facebook) to share new publications and journal updates. For 2021 we have brought on four social media editors: Davor Pavlovic, Ronald Vagnozzi, Kate Weeks, and Junjie Xiao, who will help bring more content to our social media channels.

Ensuring data integrity remains a top priority for the coming year. Our updated data sharing policy takes effect in 2021 and requires that all new submissions containing ‘omics data share the datasets in a public repository. We also have new guidelines for presentation and description of data, including graph types, figure legends and presentation of blots and gels. Please visit our author guidelines for the new requirements.

Finally, we have planned several calls for papers in 2021. These papers will be handled by a small task force of editors who are leaders in their field. If you to research in these areas, submitting papers to JMCC is a great way to put your work in front of some of the top scientists in the field. The topics and dates for submission are:

March 2021- September 2021
Topics:
1. Cardiovascular Metabolism and Inflammation
2. Cardiac Fibrosis, Regeneration and Re-engineering

September 2021 – March 2022
Topics:
1. Sarcomere protein mutations
2. Ion homeostasis/calium channels/arrhythmias

Check JMCC’s website and social media for additional detailed descriptions of each topic.

We thank our readers for your continued support of JMCC. We look forward to an even better year in 2021, bringing more cardiovascular advances to the research community.

Rong Tian, MD, PhD
Editor in Chief

Michael Regnier, PhD
 Deputy Editor

Jenny Kimbel
Managing Editor, JMCC

We’ve officially completed one year as the editorial team for JMCC, and what a year it has been! We are grateful to our associate editors, consulting editors, guest editors, reviewers and authors for your hard work and dedication to elevate JMCC and bring new cardiovascular research to the forefront during such a unique and eventful year.
The Journal of Molecular and Cellular Cardiology is pleased to announce our Editor’s selections for **2020 Papers of the Year**. These articles represent topics of great interest to the research community, with work that has generated immediate impact in the field of cardiology. You can read all four articles Open Access on the JMCC website at jmcc-online.com.

### Original Research

**Isogenic models of hypertrophic cardiomyopathy unveil differential phenotypes and mechanism-driven therapeutics**

Jamie R. Bhagwan, Diogo Mosqueira, Karolina Chairez-Cantu, Ingra Mannhardt, Sara E. Bodbin, Mine Bakar, James G.W. Smith, Chris Denning

Journal of Molecular and Cellular Cardiology, Volume 145, 2020, Pages 43-53, ISSN 0022-2828, [https://doi.org/10.1016/j.jmcc.2020.06.003](https://doi.org/10.1016/j.jmcc.2020.06.003)

**Human Purkinje in silico model enables mechanistic investigations into automaticity and pro-arrhythmic abnormalities**

Cristian Trovato, Elisa Passini, Norbert Nagy, András Varró, Najah Abi-Gerges, Stefano Severi, Blanca Rodriguez

Journal of Molecular and Cellular Cardiology, Volume 142, 2020, Pages 24-38, ISSN 0022-2828, [https://doi.org/10.1016/j.jmcc.2020.04.001](https://doi.org/10.1016/j.jmcc.2020.04.001)

### Review

**SARS-CoV-2 receptor ACE2-dependent implications on the cardiovascular system: From basic science to clinical implications**

Sonja Groß, Christopher Jahn, Sarah Cushman, Christian Bür, Thomas Thum


**Circadian influence on the microbiome improves heart failure outcomes**


REPORT ON THE XLIV AUSTRALASIAN SECTION MEETING
(DECEMBER 11-13, 2020; VIRTUAL & SATELLITE MEETING HUBS, AUSTRALIA & NEW ZEALAND)

The 44th Annual Scientific Meeting of the International Society for Heart Research (ISHR) Australasian Section was held from December 11–13th 2020, in conjunction with the 68th Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand (CSANZ). The COVID-19 pandemic saw the meeting held virtually, with some delegates being lucky enough to have the opportunity to attend the meeting in person at satellite meeting hubs in Sydney, Brisbane, and Adelaide in Australia, as well as in Wellington, New Zealand.

The virtual platform was a huge success, with over 100 delegates (and in some cases over 500) tuning into sessions across the three days. The rapid adaptation of the meeting to the comprehensive virtual platform was impressive, and congratulations must go to all of the organisers, including ISHR Australasia President Fadi Charchar and local organising committee member Enzo Porrello, for a successful event.

This year, the prestigious RT Hall Lecture was given by Dr. Paul Ridker, Director of the Centre for Cardiovascular Disease Prevention, Brigham and Women’s Hospital (MA, USA), who discussed the success of targeting inflammation using anti-cytokine therapies to prevent cardiovascular deaths. The Kempson Maddox Lecture was given by Professor Karlheinz Peter (Baker Heart and Diabetes Institute, AUS), who gave a comprehensive lecture on the pitfalls, current challenges and future opportunities in the prevention and treatment of myocardial infarction, with a focus on atherosclerotic plaque instability, anti-platelet therapy and how to prevent cardiac ischaemia and reperfusion injury. The CSANZ Basic Science Lecture was delivered by Professor Lea Delbridge (University of Melbourne, AUS), who discussed how the underlying molecular mechanisms of heart failure with preserved ejection fraction remain largely underexplored, and highlighted new domains being studied by their group. The 2020 CSANZ Ralph Reader Prize for Basic Science went to ISHR early career investigator (ECI) member Dr. Celine Santiago (Victor Chang Cardiac Research Institute, AUS), for her talk “Titin truncation provides a sensitised template for cardio-depressant effects of alcohol”. The 2020 CSANZ Ralph Reader Clinical Prize went to Dr. Chrishan Nalliah (Royal Melbourne Hospital, AUS), for his talk “Impact of continuous positive airway pressure on the atrial substrate in patients with obstructive sleep apnoea and atrial fibrillation: the SLEEP-AF substrate sub-study”.

Delegates attending the meeting at the Wellington, NZ (left) and Adelaide, AUS (right) meeting hubs.
Key themes of the ISHR Australasian section included emerging tools in cardiovascular research, the pros and cons of using genomics for precision and personalised medicine, and preclinical discovery of novel therapeutics. We were particularly pleased to welcome Professor Roger Foo (NUS, Singapore) to the meeting to present his group’s unique work on using epigenomic, rather than genomic, profiling to identify risk-conferring variants. Overall, the meeting boasted a diverse range of topics from single-cell transcriptomics, biomarker discovery, metabolic risk scores and the role of the microbiome in cardiovascular disease. We were also proud to have achieved a 50:50 ratio of male and female speakers at the meeting.

These sessions were complemented by a stimulating panel discussion about the impact of COVID-19 on research, and the role of basic scientists in furthering the understanding of how COVID-19 works and its effects on the cardiovascular system. Participating panellists included Professor Livia Hool (University of Western Australia, AUS), Professor Jamie Vandenbarg (Victor Chang Cardiac Research Institute, AUS), Professor Janna Morrison (University of South Australia, AUS), and Associate Professor Enzo Porrello (Murdoch Children’s Research Institute, AUS).

While perhaps not as immersive as the usual in-person format, the virtual platform did provide unique opportunities to enhance the meeting experience. This included the addition of podcasts to the program, as well as on-demand content, such that attendees could listen to any presentations they missed out on or wanted to hear again following the meeting. Of particular note were interviews hosted by ISHR ECI members Priscilla Prestes, Michelle Maier, and Nicola Sergienko. Priscilla and Michelle discussed the challenges faced by women building their careers in cardiovascular research with Dr. Kate Weeks (Baker Heart & Diabetes Institute, AUS), while Nicola asked Dr. Alexander Pinto and Laura Bienvenu (Baker Heart & Diabetes Institute, AUS) to share some of their experiences with being both a mentor and a mentee.

As a proud supporter of ECIs, including research students and early post-doctoral fellows, the ISHR Australasian section hosted several outstanding ECI-themed presentations during the 2020 in-person/virtual hybrid AGM. These sessions also provided ECIs with opportunities to compete for prizes. The ISHR Student Investigator Oral Presentation finalists of 2020 included: Sanuja Fernando, Kahli Jones, Khalia Primer and Alex Parker. Congratulations go to winner Khali Jones, for her talk entitled “Examining the effects of ErbB4 deletion on cardiomyocytes and cardiac endothelium in neonatal mice”. The runner-up prize went to Sanuja Fernando for her talk “Eukaryotic elongation factor 2 kinase (eEF2k) regulates foam cell formation and atherosclerosis by promoting translation and glycosylation of CD36 scavenger receptor expression in macrophages”.

In addition to the Prize Session, PhD students Nicola Sergienko, Feby Sevira, and Ruth Magaye gave outstanding presentations showcasing the calibre of up-and-coming researchers in the Free Communication session. Well done to all young researchers for their excellent presentations and responses to questions and comments from a supportive and inquisitive audience.

The ISHR Publication Prize was awarded to Gregory Quaife-Ryan, for his publication in Development entitled “β-catenin drives distinct transcriptional networks in proliferative and non-proliferative cardiomyocytes”. This year, two joint prize-winners were awarded the ISHR Post-doctoral Publication Prize: Dr. Wei-Wen Lim, for his work “Interleukin-11 is important for vascular smooth muscle phenotypic switching and aortic inflammation, fibrosis and remodelling in mouse models” (Scientific Reports, 2020) and Dr. Darnel Prakoso, for his work...
“Gene therapy targeting cardiac phosphoinositide 3-kinase (p110a) attenuates cardiac remodelling in type 2 diabetes” (American Journal of Physiology Heart Circulatory and Physiology, 2020).

Further evidence of increased support for the ECI is shown by the recent initiative from the ISHR Australasian section as they recently set up its inaugural ECI Committee. The main responsibilities of the ECI Committee will be to plan and organise ECI related events (symposium, workshops and networking) during the annual ISHR Australasian Meeting and across the calendar year. The committee will further endeavour to help spotlight issues and/or create opportunities for career development for ISHR ECI members.

The committee is made up of a great blend of ECI at different career stages and from various states within Australia. The current committee consists of Co-chairs Celine Santiago and Yow Keat Tham, Thomas Agbaedeng, Priscilla Prestes, Dan Donner, Darnel Prakoso, Nicola Sergienko, and Sheila Patel.

The Committee will be tweeting from @ISHR_AUS; follow them on twitter to keep abreast of upcoming plans and activities!

We look forward to welcoming Australasian delegates back in person at the next ISHR Australasian Section Meeting to be held August 5–8, 2021 in Adelaide, South Australia.

Dr. Celine Santiago & Dr. Yow Keat Tham, with assistance from the ISHR Australasia ECI Committee. Photos from ISHR Australasia section meeting courtesy of Libby Stavrinos, CSANZ.
Dr. Hill is a cardiologist-scientist whose research focuses on molecular mechanisms of remodeling in the disease-stressed myocardium. He graduated with an MD, PhD from Duke University. Next, he pursued postdoctoral scientific training at the Institut Pasteur in Paris, followed by clinical training in Internal Medicine and Cardiology at the Brigham and Women’s Hospital, Harvard Medical School. Dr. Hill served on the faculty of the University of Iowa for 5 years before moving in 2002 to the University of Texas Southwestern Medical Center to assume the role of Chief of Cardiology and Director of the Harry S. Moss Heart Center. Dr. Hill’s research group strives to decipher mechanisms of structural, functional, metabolic, and electrical remodeling in heart disease with an eye toward therapeutic intervention. Dr. Hill serves on numerous committees, boards, and study sections, and he lectures widely. In addition, he serves on several editorial boards, including Circulation Research: Senior Consulting Editor, American Journal of Physiology, Heart and Circulatory Physiology, and American Journal of Cardiology. He serves as Editor-in-Chief of the textbook Muscle: Fundamental Biology and Mechanisms of Disease. He has received numerous recognitions and awards, including election to the Association of American Professors; he recently served as President of the Association of University Cardiologists and chair of the Academic Council of the American College of Cardiology. Presently, he serves as Editor-in-Chief of Circulation. Dr. Hill maintains an active clinical practice focusing on general cardiology, heart failure, and hypertension.

JOSEPH A HILL, MD, PHD

Heart Failure: Two Inflammatory Tales

Winner of the 2018 Research Achievement Award

(September, 2018: NANJING, CHINA)

Calendar

Note that meeting dates may have changed because of COVID-19 considerations

- **June 29-July 1, 2021.** XXXVI Annual Meeting of the European Section. VIRTUAL MEETING. Inquiries: Alessandra Ghigo, ghigo.alessandra@gmail.com.
- **August 5-8, 2021.** XLV Annual Meeting of the Australasian Section (held jointly with the Cardiac Society of Australia and New Zealand). Adelaide, Australia.
- **September 12-16, 2021.** XXXVIII Annual Meeting of the North American Section. Denver, CO. Inquiries: Timothy McKinsey, timothy.mckinsey@ucdenver.edu.
- **December 10-11, 2021.** XXXVIII Annual Meeting of the Japanese Section. Kurume, Japan. Inquiries: Masafumi Yano yanoma@yamaguchi-u.ac.jp.
- **June 12-15, 2022.** XXIV ISHR World Congress. Berlin, Germany. Website: https://www.ishr3033berlin.de
meetings in the first half of 2021 and this leaves organizers and participants with a big loss. I am sorry for those of us who had organized scientific conferences and put so much personal effort into it. We can only hope that our ISHR World Congress will be a live event and compensate for some of the loss.

The 2020 ISHR Award winners, who could not give their lectures in 2020 will mainly do so in one of the virtual ISHR Section meeting in 2021 and then receive their plaque in an appropriate ceremony at the ISHR World Congress in Berlin. Not an adequate compensation, but better than nothing. We will soon announce the 2022 competition for ISHR Awards and are looking forward to your nominations.

In my previous letter, I noted some positive consequences of Covid-19. One was the creation of the ISHR Cardiovascular Webinar series, inaugurated April 1, 2020. It was, in my view, by far the best webinar series and also one of the first. I am deeply grateful to Davor Pavlovic (Univ of Birmingham) and Michael Shattock (King’s College London), who initiated it and to Rong Tian, Editor-in-Chief of JMCC, and the ISHR leadership for supporting it. No doubt, the first series (April 2 to June 26, 2020) was a big success with 61 speakers, a mean of 210 attendees/webinar and a total of 3000 attendees from 28 countries. For those of you who missed one and want to see it, please refer to https://www.youtube.com/channel/UCxV6dGmm-jYoEgRqWEHbSA. Kate Weeks, Jim Bell, Kim Mellor and Jeff Erickson launched an ISHR Asia-Pacific Cardiovascular Webinar Series, which ran between May and November 2020 on a bi-weekly basis. It captured a wide audience from central US to India and featured two speakers, generally one senior and one junior scientist. The ISHR-JMCC webinar series will continue in a modified form this year. The series will be hosted by the JMCC’s social media editors (Davor Pavlovic (EUR), Kate Weeks (AUS), Ron Vagnozzi (NAS) and Junjie Xiao (CHI)) and will feature presentations from the authors of each month’s Editor’s Choice article, as well as other invited speakers. They plan to hold approx. 2 webinars per month. The first webinar kicked off on 31st March, 4 pm CET. The webinar series shows not only the need for deep scientific discussion in these difficult times, but also demonstrates the enthusiasm of the heart research community. A big thanks to everybody making this a flagship ISHR project in times of Covid-19!

Kate Weeks and her industrious colleagues have established guidelines for the establishment of a standing Early Career Investigator (ECI) Committee, which will be inaugurated at the World Congress in Berlin. And both the ECI and the Mid-Career Investigators (MCI) will have an active role in the organization of the program in Berlin. Many thanks to both committees for their dedication to ISHR!

David Eisner, chairman of the Fellows of the ISHR (FISHR) Credentials Committee, has updated the FISHR guidelines and prepared for the next election. And Tish Murphy, head of the Nomination Committee, is in the final stage of organizing the election of ISHR officers. I am very grateful to both of them.

And yes, there will be a time after Covid-19 and it is rare that I look forward to a conference so intensely as I look forward to our 2022 ISHR World Congress in Berlin. We have assembled an excellent Scientific Programme Committee under the leadership of our Secretary General, Lea Delbridge, and received 130 proposals for ISHR Symposia, a record number. Burkert Pieske, the local organizer of the Congress in Berlin, and Conventus, the congress organizer, have found a great new venue after our original venue announced they would be under construction. Thus, we are well set for our next ISHR World Congress in Berlin, Germany, June 12-15, 2022. We all hope that this, at last, is a safe date. Please save the date and spread the word!

Thomas Eschenhagen, MD
President ISHR
well as Hugh and Mary Blaschko, who kept in contact with those of us who had left the lab and were scattered around the world. I still keep a folder with their letters in the top drawer of my desk. But that would be a whole new story.

References

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Acknowledgments: I am indebted to Dr. Brian D. Ross (Altadena, CA) and to Dr. Guillermo Sáez (Valencia Spain) for comments and suggestions.

(continued from page 5)

therapy for heart failure in the 21st century. He then developed a unique animal model for this and spend the next decade elucidating molecular and cellular mechanisms attributable to CRT. Among the many surprising discoveries, was that CRT acts like a myofilament Ca$^{2+}$ sensitizer, by stimulating glycolysis synthase kinase-beta phosphorylation of sarcomere proteins. A 2015 report in Science Translational Medicine showed surprisingly that daily nocturnal exposure to dyssynchrony in an otherwise synchronous failing heart improved its function and structure. The new therapy (called PITA) may help millions of patients who are not CRT candidates, and clinical trials are ongoing. Another landmark effort from his lab was the early 2000’s discovery that nitroxy, the protonated form of nitric oxide, is a positive inotrope and veno/arterial dilator with potential utility to treat heart failure. He co-founded Cardioxyl in 2005 which developed and tested novel HNO donors through to Phase II clinical trials. Cardioxyl was bought by Bristol Meyers Squibb in 2015.

In early 2000s, David undertook a major transition, melding molecular and cellular biology with his bio-engineering to elucidate heart failure mechanisms and new therapies. A major area of interest has been the regulation and role of cyclic GMP and protein kinase G in the heart. His lab first reported how the PDE5 inhibitor Viagra reduced pathological cardiac hypertrophy, fibrosis, and improved function. Ten years later, he revealed PDE9 as the other selective cGMP-PDE in heart that specifically regulates natriuretic peptide signaling. He uncovered novel targets of PKG, including the non-selective cation channel TRPC6 which laid the groundwork for a treatment of muscular dystrophy, and recently the protein TSC2 that controls the mechanistic target of rapamycin. This study revealed a potent regulatory serine that in turn controls ischemic injury, metabolism, pathological growth, and autophagy. This has implications outside the heart, notably in immune cells, and this is currently being studied with implications to immune-oncology and autoimmune disease therapy. He also continues to play a major role in clinical research aimed at revealing mechanisms and identifying clinical subtypes and treatments for HFpEF, and for RV failure with forms of pulmonary hypertension. His laboratory is home to clinicians, physician and basic scientists, and graduate students. In between his research, mentoring, and entrepreneurial activities, David is an avid clarinetist, performing chamber music in the Washington D.C. area.
IN APPRECIATION

The International Society for Heart Research (ISHR) would like to thank long-time sponsor, the Institute La Conference Hippocrate (AICH), for their support of the ISHR newsletter.

AICH is a French association that belongs to the Group SERVIER whose activity is devoted to the development and sharing of medical awareness and also helps to promote the knowledge and the proper use of drugs.

The educational grant from AICH makes possible the triennial publication of Heart News & Views, which is an invaluable tool for communication between members of the ISHR and documentation of ISHR history.