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Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

European Perspectives in Cardiology

Spotlight: Manuel Mayr, MD, PhD

"As the Technology Develops, We Will Look at Not Just How Proteins Are Expressed, But Also How They Are Modified"

Manuel Mayr, professor of cardiovascular proteomics, British Heart Foundation Centre of Research Excellence, James Black Centre, King's College London, London, England, talks to Mark Nicholls.

Proteomics is a developing discipline, and it is being used to unlock some of the remaining mysteries of cardiovascular disease. Manuel Mayr, MD, PhD, professor of cardiovascular proteomics, British Heart Foundation Centre of Research Excellence, James Black Centre, King's College London, London, England, explains, "Amazing work is done in genetics and genomics, but we need to move on to the next level and integrate genetic information with better phenotyping by postgenomic technologies. Our main aim is to concentrate on the products of the genome and not just the genetic information itself. We want to get closer to the phenotype. It is the proteins that ultimately determine function."

Professor Mayr's research focuses on how proteomics, metabolomics, and microRNA profiling can advance understanding of cardiovascular disease processes. Technology such as mass spectrometry is enabling his research group to "access these molecules of life." He says, "I think this is going to be revolutionary. Most people are familiar with genomics and genetics. Proteomics and metabolomics are not mainstream but we will see a change where more people use it and see the benefits of it."

In a recent article in *Circulation*,[1] titled "Proteomics analysis of cardiac extracellular matrix remodeling in a porcine model of ischemia-reperfusion injury," Professor Mayr and his colleagues described extracellular matrix proteins that had never been looked at in the heart before. "The reason is that they are not annotated as heart proteins but as cartilage proteins, and under normal conditions are not expressed in the heart," he says. He adds that most protein annotation is based on healthy tissue but other proteins appear in diseased tissue and can be identified using proteomics. Generally, working with novel proteins is more difficult because researchers first need to generate the tools. "Mass spectrometry allows us to analyse proteins without the constraint of whether good antibodies are available," says Professor Mayr. "This freedom to look at which proteins are actually there is a big step forward, and more people are going to take advantage of these technologies."

The role of microRNAs as cardiovascular biomarkers is another important research area for Professor Mayr and his team. Their article on plasma microRNA profiling in type 2 diabetes mellitus in *Circulation Research*[2] received the best manuscript award in 2011. "We became interested in microRNAs because they regulate protein expression. They are fine-tuning protein expression," Professor Mayr explains. "By looking at circulating microRNA networks, our aim is to identify novel biomarkers. Currently, we are assessing cardiovascular risk factors, but we do not know how individuals respond to these risk factors. Circulating microRNAs may help to better identify vulnerable patients."

On other pages...

Centre of Excellence: James Black Centre, King's College London, London, England
A multidisciplinary environment with core facilities, including genomics, proteomics, state-of-the-art microscopy, and in vivo phenotyping, directed by Professor Ajay Shah, MD, FRCP, FMedSci. **Page f112**

European Meetings Update, June 2012
European meetings for the cardiovascular clinical and research communities in June 2012. **Page f114**

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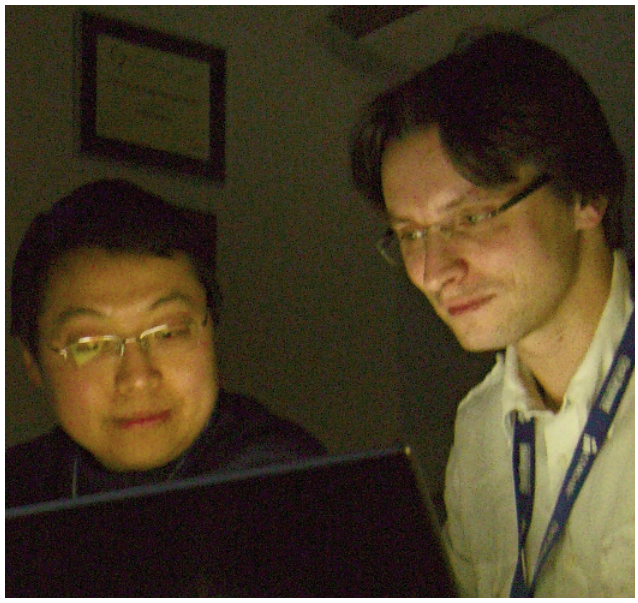

Professor Mayr analysing data with Xiaoke Yin, PhD. Photograph courtesy of Professor Mayr.

A particularly enjoyable and satisfying study for Professor Mayr was published in *Blood* in 2010.[3] It involved a proteomic effort to find a surface marker for endothelial progenitor cells. Professor Mayr says, "There was no specific marker to identify these cells unambiguously, so we applied proteomics. To our great surprise we did not find a progenitor cell marker, but a platelet-specific protein. It turned out that these so-called stem cell cultures were contaminated with platelets and that the cells in these cultures are not stem cells but macrophages incorporating platelet proteins." Although this finding was somewhat "negative," Professor Mayr adds, "for me it was a success because it demonstrated that proteomics can deliver insights not provided by other technologies. Proteomics provided an explanation for some of the inconsistencies in studies on endothelial progenitor cells."

Professor Mayr has won a number of awards and prizes, including the Michael Davies Young Investigator Award of the British Atherosclerosis Society in 2002, the inaugural Michael Davies Early Career Award from the British Cardiovascular Society in 2007, and the inaugural Bernard and Joan Marshall Research Excellence Award by the British Society for Cardiovascular Research in 2010. He was a Young Investigator Finalist for the American Heart Association Council on Functional Genomics and Translational Biology in 2009 and Arteriosclerosis, Thrombosis and Vascular Biology in 2010.

"What Got Me Up in the Morning Was the Curiosity to Find Something New"

Born in Linz, Austria, Professor Mayr graduated from the University of Innsbruck Medical School, Innsbruck, Austria, in 1999 "*sub ausspiciis presidentis rei publicae*," the highest distinction awarded for academic education. He developed his interest in cardiology and cardiovascular research while investigating the role of heat shock proteins in atherosclerosis for his thesis with Professor Georg Wick, MD, at the Institute of Experimental Pathology. This work resulted in articles in *Circulation* in 1999[4] and 2000.[5] At this point, Professor Mayr decided to forego further clinical training and pursue research. "I thought it was better to go abroad to do a PhD, and that is how I came to the United Kingdom," he says. "It was a big decision because it meant leaving my medical training behind and going from a clinical career to basic science. But I was so interested in research. What got me up in the morning was the curiosity to find something new."

Professor Mayr began his postdoctoral studies with Professor Qingbo Xu, MBBS, MD, PhD, at the Institute of Biomedical Aging Research of the Austrian Academy of Sciences, where he worked on animal models and cellular signalling in response to biomechanical stress. In 2001, he moved with Professor Xu to the Department of Cardiac and Vascular Sciences at St. George's Hospital Medical School, London, where he developed his proteomic skills and obtained his PhD. This move involved relocating with his wife (whom he met at medical school in Innsbruck and whom is also part of his research group) and family (they have 3 daughters, now aged between 3 and 11 years) to a new country from his native Austria.

After a sabbatical in the lab of Professor Peipei Ping, PhD, at the University of California, Los Angeles, CA, in 2006, Professor Mayr was appointed as a lecturer in the Division of Cardiovascular Sciences at King's College London. He is now professor in cardiovascular proteomics and a senior fellow of the British Heart Foundation, and is involved in cardiovascular basic science and translational studies using proteomics.

Professor Mayr says, "Proteomics is not an off-the-shelf technology. It requires a lot of tweaking, tuning of the methods, and adapting it to cardiovascular disease. This is our strength and expertise. We are exclusively focussed on cardiovascular proteomics. As a result of this expertise, we are involved in a lot of collaborations within the centre and across the United Kingdom and internationally."

A number of people have helped shape Professor Mayr's career and continue to influence and inspire him. Initially, it was Professor Wick in Innsbruck, and later, Professor Xu. "To have a successful career, you are really dependent on good mentors, and I had a lot of them," he says. "Professor Xu was the key for my transition to faculty position and getting the funding for proteomics. I think initially your mentoring is very much local, but later it becomes more international. In this respect, the Functional Genomics and Translational Biology Council of the American Heart Association was key for identifying international mentors. This relatively new council reaches out to European scientists and welcomes active participation by younger scientists through its Early Career initiative." Professor Mayr is also grateful for mentoring provided by Professor Jennifer Van Eyk, MD, at John Hopkins University, Baltimore, MD, who works in cardiac proteomics. "She gave me good advice and we have had really interesting scientific discussions," says Professor Mayr.

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Professor Stefan Kiechl, MD, and Professor Johann Willeit, MD, from Innsbruck have been long-term collaborators with Professor Mayr since his days at medical school. He says, "Without them, much of the work we have been able to publish would not have been possible. We have collaborated for almost 15 years. Combining their population-based study with our latest technology in proteomics, metabolomics, and microRNA profiling is extremely exciting and has the potential to identify new biomarkers. The Bruneck study is like a mini Framingham study. The cohort is extremely well phenotyped, and that is incredibly valuable."[6]

Professor Mayr advises people wanting to follow a career in research to "be prepared to move to places where you can do the best research." His future plans are simple. He says, "I just want to do more research and see how the technology will take us to the next level. At present our research is focussed on protein identification and quantitation, but as the technology develops we will look at not just how proteins are expressed but also how they are modified. I have a good team with some very bright people, and my next challenge will be not only to produce good articles but also to train the next generation of scientists and give young people a good start in their career. I am grateful for the good mentoring I have received, and I will try to mentor other people and hopefully give them the help and advice they need."

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Mark Nicholls is a freelance medical journalist.

Professor Mayr's research group at the James Black Centre, King's College London, includes 6 postdoctoral researchers (Ursula Mayr, MD, Anna Zampetaki, PhD, Xiaoke Yin, PhD, Philipp Skroblin, PhD, Javier Barallobre-Barreiro, PhD, and Katarzyna Dudek, PhD); 1 bioinformatician (Sarah Langley, PhD); 3 PhD students (Nada Abdulkareem, MD, Ignat Drozdov, MSc, and Patricia Gyambibi-Barnett, MSc); and a lab manager (Qiuru Xing, MSc). This photograph of his group shows from left to right: Drs Barallobre-Barreiro and Anna Zampetaki (1st row), Dr Mayr, MD, and Qiuru Xing (2nd row), Ignat Drozdov and Patricia Gyambibi-Barnett (3rd row), Professor Mayr and Dr Abbdulkareem (4th row), and Dr Yin (back row). Professor Mayr's research is primarily funded by the British Heart Foundation. Photograph courtesy of Professor Mayr.

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Centre of Excellence: James Black Centre, King's College London, London, England

Sharing Expertise and Supporting Projects Across Departments and Specialist Areas

Manuel Mayr, MD, PhD, professor of cardiovascular proteomics, British Heart Foundation Centre of Research Excellence, James Black Centre, King's College London, London, England, and member of the steering group of the British Heart Foundation Centre of Research Excellence talks about the James Black Centre to Mark Nicholls.

The £30 million James Black Centre, King's College London, London, England, opened in 2007 and is named after pharmacologist, Sir James Black, FRS (see http://circ.ahajournals.org/content/117/8/f43), who shared the Nobel prize for Physiology or Medicine in 1988 for discovering important principles for drug treatment. It provides a multidisciplinary environment with core facilities, including genomics, proteomics, state-of-the-art microscopy, in vivo phenotyping, and magnetic resonance imaging, and it is part of the King's College London Cardiovascular Division and the British Heart Foundation Centre of Research Excellence. The centre is directed by Professor Ajay Shah, MD, FRCP, FMedSci (see http://circ.ahajournals.org/content/122/5/f25), who also heads the King's College London Cardiovascular Division. As 1 of the largest research divisions within the health schools of King's College London, with 220 research workers (including 35 principal investigators and >70 PhD/MD students), the King's College London Cardiovascular Division is based on the 3 hospital campuses of the King's College Schools (St. Thomas's, Denmark Hill and Guy's, and Waterloo) and is part of the British Heart Foundation Centre of Research Excellence.

With £9 million of funding from the British Heart Foundation, the British Heart Foundation Centre of Research Excellence was established in April 2008 to build upon the cardiovascular and related noncardiovascular strengths at King's College London, and provide a highly collaborative, multidisciplinary environment that catalyses the pursuit of imaginative and innovative cardiovascular research programmes. Clinicians, clinician scientists, basic scientists, imaging specialists, and biologists from across the health schools of King's College London (ie, the Cardiovascular Division, the Randall Division of Cell and Molecular Biophysics, and the Imaging Sciences Division) work together to advance the early diagnosis, prevention, and treatment of heart diseases, and to deliver research training for clinical and nonclinical scientists. A major emphasis is the translation of fundamental lab advances to the clinical arena to lead to therapeutic advances for atherosclerosis, cardiac protection, and cardiac failure.

The research activities at King's College London British Heart Foundation Centre of Research Excellence focus on cardiac and vascular biomedicine, with a major emphasis on cellular and molecular signalling. Eight complementary and interacting integrated research themes employ a bench-to-bedside approach. Each area is led by senior experts within the centre. Within the cardiac biomedicine area, the Muscle Cell Biology group, led by Professor Mathias Gautel, MD, PhD, investigates the mechanisms that organise, regulate, and remodel the sarcomere, and how sarcomeres crosstalk to mechanisms controlling muscle growth or atrophy.[1] The Signalling in Myocardial Ischaemia group is led by Professor Metin Avkiran, BSc, PhD, DSc, FISHR, and Professor Michael Marber, MBBS, PhD, FRCP. Professor Marber's group investigates the processes that contribute to myocardial injury during ischaemia and reperfusion.[2] Professor Avkiran's Molecular Cardiology Group aims to integrate physiological and pharmacological approaches with biochemical and molecular biological techniques to study mechanisms underlying cardiac injury and dysfunction.[3] The Oxidative Stress and Redox Signalling in Cardiovascular Disease group, led by Professor Shah, studies the role of NADPH oxidases and redox-regulated pathways in the development of cardiac hypertrophy and failure, and vascular dysfunction.[4]

Within the vascular biomedicine area, the Stem Cells and Vascular Disease basic science research group, led by Professor Qingbo Xu, MBBS, MD, PhD, elucidates the molecular mechanisms underlying cardiovascular diseases, especially stem cells and atherosclerosis.[5] The research group on Vascular Risk and Dysfunction, led by Professor Phil Chowienczyk, BSc, and Professor Lalit Kalra, MD, PhD, relates to the in vivo assessment of arterial structure and function in humans to elucidate mechanisms leading to arterial disease and interventions to prevent and treat arterial disease.[6] The Vascular Cell Biology research group, led by Professor Anne Ridley, PhD, and Professor Cathy Shanahan, PhD, investigates the molecular regulation of the vascular smooth muscle cell phenotype and how it relates to vascular dysfunction in diseases such as atherosclerosis, diabetes mellitus, hypertension, chronic renal failure, and ageing.[7]

The Cell and Molecular Biophysics group is led by Professor Malcolm Irving, FRS, while the Cardiovascular Imaging group is led by Professor Eike Nagel, MD, PhD, and Professor Reza Razavi, MD.

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Left, The James Black Centre, King's College London, London, England. Right, Central staircase in the James Black Centre. Photographs courtesy of Professor Mayr.

The ethos of the James Black Centre and the British Heart Foundation Centre of Research Excellence is interdisciplinary research, with groups sharing expertise and supporting projects across departments and specialist areas.

Manuel Mayr, MD, PhD, professor of cardiovascular proteomics at the James Black Centre, sits on the steering group of the British Heart Foundation Centre of Research Excellence and explains, "The centre brings together very good groups doing research on cardiovascular stem cells, cardiac hypertrophy, and cardiac ischaemia, and there is a strong focus on being interdisciplinary. Collaborations with the imaging division at King's College and with the Randall Institute are encouraged, so the British Heart Foundation Centre of Research Excellence is not just about cardiovascular research, but also integrating other technologies into this research area. That has proven very productive and opens up a lot of new collaborations and other research interests." In terms of his proteomics group, he says, "We have many collaborations, and because we are embedded in the cardiovascular division and focussed on cardiovascular disease, we can give other people better support in their research projects. Research is getting so complex that you rarely find all the expertise in 1 group, so you have to work with people across disciplines, go outside your comfort zone and into areas you know nothing about, and get people on board who do."

Professor Shah echoes these comments and says, "The work undertaken by Professor Mayr and his group is an excellent example of how valuable core expertise is in specific areas within the British Heart Foundation Centre (in this case, proteomics) and how interdisciplinarity leads to high-impact research."

Professor Mayr reflects on the legacy of Professor Black and recalls attending 1 of his lectures when he first joined King's College London. He says, "He was a real role model. He was inspiring. They had little technology in those days, yet they came up with all these potent drugs. It is now up to our generation with our much better technology to take on the challenge to advance our knowledge."

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Mark Nicholls is a freelance medical journalist.

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European Meetings Update

June, 2012

1 to 2 June
European-Ukrainian School "Cardiovascular prevention and rehabilitation"
Lutsk, Ukraine
For further details, contact:
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2 to 5 June
17th International Vascular Biology Meeting—IVBM 2012
Wiesbaden, Germany
For further details, contact:
http://www.ivbm2012.net/

5 to 8 June
Cardio Alex 2012
Cairo, Egypt
For further details, see:
http://www.cardioalex.com/

7 to 8 June
9th International Symposium on Stem Cell Therapy and Cardiovascular Innovations
Madrid, Spain
For further details, see:
http://www.cardiovascularcelltherapy.com/

7 to 9 June
4th Annual CMR Course
Munich, Germany
For further details, see:
http://www.cmr-course.de/

7 to 9 June
Anti-Thrombotic Therapy—Update 2012
Sophia Antipolis, France
For further details, see:
http://www.escardio.org/education/live-events/courses/anti-thrombotic-therapy/Pages/programme.aspx

7 to 10 June
The 10th World Congress of the International Society for Adaptive Medicine
Bucharest, Romania
For further details, see:
http://www.isam2012.info/ISAM/Welcome.html

11 to 12 June
Arrhythmia and Device Therapy in Daily Practice—A Case-based Approach
Sophia Antipolis, France
For further details, see:
http://www.escardio.org/education/live-events/courses/heart-rhythm/Pages/case-based-arrhythmia-device-practice.aspx

11 to 13 June
Cardiology and Vascular Medicine
Rotterdam, the Netherlands
For further details, see:
http://www.escardio.org/education/live-events/courses/cardiology-vascular-update/Pages/programme.aspx

13 to 13 June
EHRA Certification Exam on Cardiac Pacing and Implantable Cardioverter Defibrillators
Nice, France
For further details, see:
http://www.escardio.org/communities/EHRA/accreditation/Pages/cardiac-pacing-icds.aspx

13 to 15 June
Annual Congress of the Swiss Society of Cardiology 2012
Lausanne, Switzerland
For further details, see:
http://www.congrex.ch/fr/sgk2012.html

13 to 16 June
Cardiostim 2012—18th WORLD CONGRESS
Nice, France
For further details, see:
http://www.cardiostim.com/

14 to 14 June
EHRA Certification Exam in Invasive Cardiac Electrophysiology Certification
Nice, France
For further details, see:
http://www.escardio.org/communities/EHRA/accreditation/Pages/electrophysiology.aspx

14 to 15 June
Moscow International Forum of Cardiology
Moscow, Russia
For further details, contact
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15 to 16 June
Nordic Cardiovascular Imaging meeting 2012
Copenhagen, Denmark
For further details, see
http://nordicci.org/scientific-programme/

19 to 22 June
11th International Conference of the Jordan Cardiac Society
Petra, Jordan
For further details, see
http://www.jordancardiac.com/cms/

27 to 27 June
iCi 2012—Interventional Imaging
Frankfurt am Main, Germany
For further details, see
http://www.ici-congress.org/

27 to 29 June
9èmes Journées Tuniso—Européennes de Cardiologie Pratique
Sousse, Tunisia
For further details, see
http://www.jtecp.org/fr/index.php

28 to 30 June
CSI 2012—Catheter Interventions in Congenital and Structural Heart Diseases
Frankfurt am Main, Germany
For further details, see
http://www.csi-congress.org/

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