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Professor Jules Hancox Physiology, Pharmacology and Neuroscience has been awarded a University of Bristol Research Fellowship (URF) to enable him to carry out a dedicated research project for twelve months during the academic year 2017/2018. Professor Hancox holds the Chair of Cardiac Electrophysiology and is also an Honorary Professor at the University Hospitals Bristol NHS Trust. Professor Hancox has a long-standing interest in investigating the basis of the electrical activity of the atrioventricular (AV) node and in the electrophysiology and pharmacology of the hERG potassium channel, which plays an important role in drug-induced arrhythmias and in the congenital ‘Short QT syndrome’. His present focus is to understand the basis of congenital arrhythmias associated with sudden death. In this respect he uses a ‘dynamic’ approach.

Within the last two decades, a rare congenital arrhythmia condition called the “Short QT Syndrome” (SQTS) has been discovered and linked to ion channel gene mutations that lead to abbreviation of action potentials (the physiological electrical events) of atrial and ventricular myocytes. The resulting changes lead to increased susceptibility to atrial and ventricular arrhythmias and to the risk of sudden arrhythmic death. Together with collaborators in both Bristol & Manchester, Jules has used a combination of electrophysiology and mutagenesis to study how SQTS mutations alter potassium ion channel currents. Their data have been incorporated into human cardiac computer models and have identified likely arrhythmia substrates in different forms of the SQTS. Moreover, they have explored the effectiveness of existing antiarrhythmic drugs and novel strategies against the deleterious changes produced by individual mutations in the syndrome. SQTS patients are commonly treated with implantable defibrillators and the development of adjunct pharmacology may help reduce the likelihood of patients who have devices needing defibrillation shocks. Interestingly, Jules published in vitro work on one drug was supported by subsequent results obtained elsewhere involving SQTS patients.

“The costs of generating and keeping colonies of genetically modified lagomorph or larger rodent models are remarkably high, so we’ve adopted an alternative approach to reproduce experimentally the electrophysiological changes in the SQTS: the ‘dynamic’ clamp technique”, Jules explains. The dynamic clamp technique involves recording action potentials from single cardiac myocytes from an appropriate model species and then replacing, in real-time, the activity of a native ion channel with one generated by a computer model.
Jules and Professor Clive Orchard obtained funding from the BHF to apply the technique to the SQTS: “Dynamic clamp is probably one of the most exciting approaches currently available for cellular electrophysiology” enthuses Jules. “Different systems are available, but the one we’ve gone for with repolarisation disorders in mind is called the ‘Cybercyte’. This has been developed in the USA by Dr Randall Rasmusson and his team at Cytocybernetics. We’ve worked with them and our collaborators in Manchester to incorporate potassium channel models that describe three different forms of the SQTS and Dr Rasmusson came over from the States to get the system up and running.

It forms a basic science bridge that enables us to understand the mechanisms linking epidemiological and genetic studies to problems encountered in the clinic.”

Jules is quick to point out the wider applications for using dynamic clamp in cardiac research in Bristol. “Dynamic clamp has wide applications: for example, it is also being used here in heart failure related research on an MRC Programme that’s led by Prof Mark Cannell. Also, Bristol is the regional centre for inherited conditions, including congenital arrhythmias, and Dr Graham Stuart, lead cardiologist for the inherited cardiac conditions (ICC) service, and Prof Ruth Newbury-Ecob, lead clinical geneticist, have welcomed Dr Andrew James and myself into ICC meetings, where the synergy between clinical and basic science expertise has been mutually beneficial. Dr Stuart and I are currently collaborating on SQTS research and we have been jointly responsible for proposing SQTS as an eligible disorder for the 100,000 Genomes initiative. With the recent arrival to PPN in Bristol of Dr Steve Harmer, who can make person-specific induced pluripotent stem-cell (iPSC) derived myocytes, we have the prospect of combining the use of iPSC-derived myocytes from patients with arrhythmia syndromes with dynamic clamp. In time we should be able to conduct patient- and mutation- specific studies to characterize disease causing mutations and to test drugs against these. iPSC derived myocytes can lack some properties of adult cardiac myocytes and with dynamic clamp we can replace the missing ionic current(s). Of course, we will also want to do the kind of experiments on adult myocytes that we’ve been doing on the SQTS and as long as the relevant mammalian model species continue to be available to us, we hope to do so. The future is full of exciting potential.”
TWO veteran fundraisers have been honoured by the British Heart Foundation for dedicating more than 40 years to the charity.

Dot Ings and Roy Brookman, who helped set up the Chippenham and District fundraising branch of the charity, received an award last Thursday from chief executive Simon Gillespie and Professor Gianni Angelini for outstanding contribution.

Full article here

http://www.gazetteandherald.co.uk/
The STEM for Britain event is an opportunity for PhD students and post-docs to present their research to members of parliament. The event this year was sponsored by Research Councils and many scientific societies, including The Physiological Society and the Royal Society for Biology and was hosted by Stephen Metcalf MP and the Parliamentary and Scientific Committee. The participants were selected from submitted abstracts and CVs. There were five scientists from Bristol University (two engineers, one physicist, one mathematician and one from the Medical School). Dr Helen Williams a research Fellow working in vascular Biology, Level 7 of the BRI was invited to participate.

Helen presented a poster which was suitable for a lay person audience. The work was a summary of her recent research showing that WISP-1 reduces atherosclerosis in a mouse model.

Surprisingly, the poser session was extremely busy. Helen says “it was the busiest poster session I have ever taken part in, with a constant stream of visitors including judges and representatives from industry and the societies sponsoring the event, resulting in lots of useful questions and conversation”. She continues “as the audience was so diverse it was a really great opportunity to engage with those from other specialities and see things from a fresh perspective”. Sadly, there were not many MPs in attendance, as parliament was discussing the response to ‘the Salisbury incident’ that afternoon.

I would really recommend the event, it was a great opportunity to present to a different audience, engage with parliament and meet and exchange ideas with other enthusiastic scientists.
Awards & Prizes

Professor Suleiman elected Fellow of the Physiological Society
The Trustees of The Physiological Society have approved Prof Suleiman in becoming a Fellow of The Society, in recognition of his continuous and active service to The Society and to the discipline. He is now eligible to use the FPhysiol designation. Prof Suleiman was first elected as a full member of the Society in 1992. http://www.physoc.org/become-a-member

The Physiological Society was founded in 1876 ‘for mutual benefit and protection’ of the physiological community. “The first members met for dinners around London to discuss business, and founded the Journal of Physiology within two years”. For more details about its origins, see: History of the Physiological Society during its First Fifty Years, 1876-1926 Part 1 was published in the J Physiol. 1927; 64(3 Suppl): 1–76. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1515042/

Martin Lewis & Katie Hall awarded oral & poster prizes at international meeting
Dr Martin Lewis (MRC Clinical Research Fellow) and Katie Hall (3rd Year Intercalating in Health Sciences iBSc) participated in the 5th European Section meeting of the International Academy of Cardiovascular Sciences (IACS-ES) held between May 23 - 26, 2018 at Smolenice Castle - The Congress center of the Slovak Academy of Sciences, Bratislava, Slovakia. Martin was awarded the first prize of €200 for oral presentation (Early Career Investigators Competition). Katie was awarded poster prize of €150 For the Young Investigator Competition.

European Society of Cardiology Training Fellowship
Dr Bostjan BERLOT from Ljubljana University Hospital, Slovenia has won a 12-month training grant from the European Society of Cardiology to train in Cardiac MRI at the Bristol Heart Institute. Dr Berlot will be supervised by Dr Chiara Bucciarelli-Ducci.
Recent Impact Publications

♥ Radial-Artery or Saphenous-Vein Grafts in Coronary-Artery Bypass Surgery

Dr Umberto Benedetto (pictured below with Prof Angelini) is the first co-author of a paper published recently in NEJM about the benefit from favouring the radial artery over vein graft in coronary bypass surgery. Bristol BRC is cited as a sponsor and Prof Angelini is also amongst senior authors (see publication details below).

By merging high quality clinical data this paper provides a unique opportunity to answer important research questions which cannot be addressed in randomized trials for various reasons (costs, large sample size, long follow-up, ethical issues). Our research group has a leading role in this field. This paper has already 4K downloads and it scored above 92% among all time NEJM papers.


♥ Antihypertensive treatment, blood pressure & exercise

A UoB team led by Dr Emma Hart (photographed with 1st author Ben Chant) has recently had an article accepted for publication in Hypertension (see abstract below). The article will be available soon and will be accompanied by an Editorial.

Original Article

Antihypertensive Treatment Fails to Control Blood Pressure During Exercise

Benjamin Chant, Majda Bakali, Thomas Hinton, Amy E. Burchell, Angus K. Nightingale, Julian F.R. Paton, Emma C. Hart

See Editorial Commentary, pp xxx-xxx

Abstract—An exaggerated blood pressure (BP) response to maximal exercise is an independent risk factor for cardiovascular events and mortality. It is unclear whether treating BP to guideline recommended levels could normalize the rise in BP during exercise, which is mediated by the metaboreflex. We aimed to assess the BP response to incremental exercise testing and metaboreflex activation in treated–controlled hypertension (n=16), treated–uncontrolled hypertension (n=16), and untreated hypertension (n=11) and 16 control participants with normal BP (n=16). All groups were matched for age and body mass index. BP was measured during an incremental V̇O2 peak test on a cycle ergometer and during metaboreflex isolation using postexercise ischemia. Data were analyzed using 2-way ANOVA with Tukey test for multiple comparisons. Aerobic fitness was similar among groups (P=0.97). The rise in absolute systolic BP from baseline at peak exercise was similar in controlled, uncontrolled, and untreated hypertension but greater compared with normotensive controls (Δ71±3, 81±7, 79±8.5 versus 47±5 mmHg; P=0.0001). Metaboreflex sensitivity was also similar in controlled, uncontrolled, and untre:nt hypertension but augmented compared with normotensive controls (Asystolic BP: 21±2, 28±2, 25±3 versus 12±2 mmHg; P<0.0001). An amplified pressor response to exercise occurred in patients taking antihypertensive medication, despite having controlled BP at rest and was potentially caused (in part) by enhanced metaboreflex sensitivity. Poor BP control during exercise, partially mediated by the metaboreflex, may contribute to the heightened risk of an adverse cardiovascular event even in treated–controlled patients. (Hypertension. 2018;72:00-00. DOI: 10.1161/HYPERTENSIONAHA.118.11076.) • Online Data Supplement
‘Microsphere’ protein could help 50 per cent of patients who have heart bypass surgery failure

A new £147,000 research project funded by Heart Research UK aims to help 50 per cent of patients who suffer from failed heart bypass surgery, saving them from further invasive surgery and potentially fatal heart attacks.

The project, led by Professor Sarah George, Professor of Cardiovascular Signalling from the Bristol Medical School and Bristol Heart Institute at the University of Bristol will look at how to prevent the failure of leg vein grafts used to treat blocked coronary arteries. For the full article please see


Special Seminar and drinks social with Stephen Harmer

Special Seminar and networking opportunity (drinks social) with Stephen Harmer, recently appointed to the School of Physiology, Pharmacology & Neuroscience. Steve does lots of cool stuff with iPSCs, proteomics, ion channels and trafficking to study inherited cardiac arrhythmias and the regulation of cardiac ion channels “Ion channel trafficking and the long QT syndrome”.

2 pm Thu 21st June, Biomedical Sciences Building, C42 (drinks social from 3 pm in D1/D3)

https://www.ncbi.nlm.nih.gov/pmc/?term=Harmer+S%5Bauthor%5D

All welcome.

For more information please contact Dr Andrew F. James: a.james@bristol.ac.uk
The Steering Group of the Bristol Heart Institute

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- Prof Robert Tulloh Consultant Paediatric Cardiologist
- Collette Sheahan RED liaison

If you have anything you wish to discuss in relation to the newsletter please contact Saadeh Suleiman (m.s.suleiman@bristol.ac.uk).

Please send comments, videos, publications, events, news etc. to Clair.Dunbavand@bristol.ac.uk to populate the website.