Cardiovascular Science Projects 2016

Supervisors		Project Title	Relevant Publications/ Description
Professor Charalambos Antoniades	Professor Keith Channon	Exploring the role of vascular redox signalling in human atherosclerosis progression	This is an exciting project examining the molecular mechanisms of atherosclerosis progression in humans. The study will build on the Oxford CABG Bioresource (OCB) cohort, which includes a bioresource of human vascular and myocardial tissue from ~900 patients who underwent cardiac surgery, with simultaneous extensive molecular, structural and functional phenotyping of their arterial tree. The project will include prospective advanced vascular imaging using computerised tomography angiography as means of characterising changes in atherosclerotic plaque structure/composition as well as intima hyperplasia, over time. Using a translational approach the project will also include mechanistic experiments using ex vivo models of human vessels and other experimental approaches, to investigate the role of vascular redox signalling directly in the pathogenesis of human vascular disease. 1. Antonopoulos AS, Margaritis M, Coutinho P, Shirodaria C, Psarros C, Herdman L, Sanna F, De Silva R, Petrou M, Sayeed R, Krasopoulos G, Lee R, Digby J, Reilly S, Bakogiannis C, Tousoulis D, Kessler B, Casadei B, Channon KM, Antoniades C. Adiponectin as a link between type 2 diabetes and vascular NADPH oxidase activity in the human arterial wall: the regulatory role of perivascular adipose tissue. Diabetes. 2015 Jun;64(6):2207-19. 2. Antoniades C, et al; Bakogiannis C, Leeson P, Guzik TJ, Zhang MH, Tousoulis D, Antonopoulos AS, Demosthenous, M, Marinou K, Hale A, Paschalis A, Psarros C, Triantafyllou C, Bendall J, Casadei B, Stefanadis C, Channon KM. Rapid, direct effects of statin treatment on arterial redox state and nitric oxide bioavailability in human atherosclerosis via tetrahydrobiopterin-mediated endothelial nitric oxide synthase coupling. Circulation. 2011 Jul 19;124(3):335-45.
Professor Charalambos Antoniades	Professor Keith Channon	Development of non-invasive tools to study the cross-talk between the	This project will build on an ongoing translational programme of work that led to the discovery of new communication links between the vascular wall and its surrounding perivascular fat. By using a novel, recently patented technology

		arterial wall and perivascular fat in human coronary atherosclerosis	studying these interactions, the project will explore the ability of non-invasive imaging by computerised tomography to provide functional in addition to structural information on the degree of vascular inflammation and atherosclerotic plaque composition in the human coronaries. The project will also use intravascular ultrasound (IVUS) and/or optical coherence tomography (OCT) to further explore the applicability of the new technology in acute coronary syndromes from the OXAMI project. Finally, using ex vivo models of human tissue and other translational approaches currently used in the Oxford CABG Bioresource (OCB), the study will provide novel insights into the biological interpretation of non-invasive/invasive imaging in humans. 1. Margaritis M, Antonopoulos AS, Digby J, Lee R, Reilly S, Coutinho P, Shirodaria C, Sayeed R, Petrou M, De Silva R, Jalilzadeh S, Demosthenous M, Bakogiannis C, Tousoulis D, Stefanadis C, Choudhury RP, Casadei B, Channon KM, Antoniades C. Interactions between vascular wall and perivascular adipose tissue reveal novel roles for adiponectin in the regulation of endothelial nitric oxide synthase function in human vessels. Circulation. 2013 Jun 4;127(22):2209-21 2. Antonopoulos AS, Margaritis M, Coutinho P, Digby J, Patel R, Psarros C, Ntusi N, Karamitsos TD, Lee R, De Silva R, Petrou M, Sayeed R, Demosthenous M, Bakogiannis C, Wordsworth PB, Tousoulis D, Neubauer S, Channon KM, Antoniades C. Reciprocal effects of systemic inflammation and brain natriuretic peptide on adiponectin biosynthesis in adipose tissue of patients with ischemic heart disease. Arterioscler Thromb Vasc Biol. 2014 Sep;34(9):2151-9 3. Shields KJ, Barinas-Mitchell E, Gingo MR, Tepper P, Goodpaster BH, Kao AH, Manzi S, Sutton-Tyrrell K. Perivascular adipose tissue of the descending thoracic aorta is associated with systemic lupus erythematosus and vascular calcification in women. Atherosclerosis. 2013 Nov;231(1):129-35
Professor Shoumo	Dr Akane Kawamura	Developing safe anticoagulants by targeting the contact system using tick	1. Renné, T., Schmaier, A.H., Nickel, K.F., Blombäck, M. & Maas, C. In vivo roles of factor XII. Blood 120, 4296 4303 (2012).

Bhattacharya	Professor Manjunatha Kini (National University of Singapore)	venom peptides	2. Bjorkqvist, J., Nickel, K.F., Stavrou, E. & Renne, T. In vivo activation and functions of the protease factor XII. Thromb Haemost 112, 868-75 (2014). 3. Chen, W., Carvalho, L.P.D., Chan, M.Y., Kini, R.M. & Kang, T.S. Fasxiator, a novel factor XIa inhibitor from snake venom, and its site-specific mutagenesis to improve potency and selectivity. J. Thromb. Haemost. 13, 248-261 (2014). 4. Koh, C. Y., et al. (2007). "Variegin, a novel fast and tight binding thrombin inhibitor from the tropical bont tick." J. Biol. Chem. 282(40): 29101-29113. 5. Koh, C. Y. and R. M. Kini (2012). "From snake venom toxins to therapeutics - Cardiovascular examples." Toxicon 59(4): 497-506.Toxicon, 59 (2012) 497-506.83
Professor Shoumo Bhattacharya	Professor David Greaves and Dr Akane Kawamura	Combinatorial targeting of the atherogenic chemokine network using novel tick venom peptides	1. White, G. E., et al. (2013). "CC chemokine receptors and chronic inflammation--therapeutic opportunities and pharmacological challenges." Pharmacol Rev 65(1): 47-89. 2. Zernecke, A. & Weber, C. Chemokines in atherosclerosis: proceedings resumed. Arteriosclerosis, Thrombosis, and Vascular Biology 34, 742-750 (2014). 3. Bursill, C.A., Choudhury, R.P., Ali, Z., Greaves, D.R. & Channon, K.M. Broad-spectrum CC-chemokine blockade by gene transfer inhibits macrophage recruitment and atherosclerotic plaque formation in apolipoprotein E-knockout mice. Circulation 110, 2460-2466 (2004). 4. Deruaz, M. et al. Ticks produce highly selective chemokine binding proteins with anti-inflammatory activity. Journal of Experimental Medicine 205, 2019-2031 (2008). 5. Copin, J.-C. et al. Treatment with Evasin-3 reduces atherosclerotic vulnerability for ischemic stroke, but not brain injury in mice. J. Cereb. Blood Flow Metab. 33, 490-498 (2013).
Associate Professor		Mitochondrial function and ion-channel regulation in arterial chemoreceptors.	1. Oxygen sensitivity of mitochondrial function in rat arterial chemoreceptor cells. Buckler KJ, Turner PJ. J Physiol. 2013 Jul 15;591(Pt 14):3549-63.

Keith Buckler			2. TASK channels in arterial chemoreceptors and their role in oxygen and acid sensing. Buckler KJ. Pflugers Arch. 2015 May;467(5):1013-25.
Associate Professor Carolyn Carr		Growing human iPS-derived cardiomyocytes in 3D in a bioreactor for pharmacological testing	1. Carpenter L*, Carr CA*, Yang CT, Stuckey DJ, Clarke, K, Watt, SM; "Efficient Cardiac Differentiation of Human Induced Pluripotent Stem Cells Which Can Provide Protection Against Myocardial Infarction in Rat Heart", Stem Cells and Development, 2012, 21, 977 2. Bruyneel A, Carr CA; Novel Biomimetic Bioreactor for the Recellularisation of Decellularised Hearts Under Synchronised Electrical and Mechanical Stimulation, Tissue Engineering Part A. September 2015, 21(S1): S386 3. Chen Q, Bruyneel A, Carr CA, Czernuszka, JT; "Bio-mechanical Properties of Novel Bi-layer Collagen-Elastin Scaffolds for Heart Valve Tissue Engineering" Proc Engineering, 2013, 59, 247-254
Dr Ricardo Carnicer	Professor Barbara Casadei	The role of nitric oxide synthase and its cofactor BH4 in diabetic cardiomyopathy	1. Bugger, H. and E. D. Abel (2014). "Molecular mechanisms of diabetic cardiomyopathy." Diabetologia 57(4): 660-671. 2. Carnicer, R; Hale, AB; Suffredini, S; Liu, X; Reilly, S; Zhang, MH; Surdo, NC; Bendall, JK; Crabtree, MJ; Lim, GB; Alp, NJ; Channon, KM; Casadei, B. (2012). Cardiomyocyte GTP cyclohydrolase 1 and tetrahydrobiopterin increase NOS1 activity and accelerate myocardial relaxation. Circulation Research 111(6): 718-727. 3. Simon, JN; Duglan, D; Casadei, B; Carnicer, R. (2014). Nitric oxide synthase regulation of cardiac excitation contraction coupling in health and disease. Journal of Molecular and Cellular Cardiology 73: 80-91.
Professor Barbara Casadei		NOS1AP and ventricular arrhythmogenesis: myocardial and neural determinants (with DJ Paterson & N Herring)	1. Lu CJ, Hao G, Nikiforova N, Larsen HE, Liu K, Crabtree MJ, Li D, Herring N, Paterson DJ. CAPON modulates neuronal calcium handling and cardiac sympathetic neurotransmission during dysautonomia in hypertension. Hypertension. 2015 Jun;65(6):1288-97. 2. Kolder IC, Tanck MW, Postema PG, Barc J, Sinner MF, Zumhagen S, Husemann A, Stallmeyer B, Koopmann TT, Hofman N, Pfeufer A, Lichtner P, Meitinger T, Beckmann BM, Myerburg RJ, Bishopric NH, Roden DM, Kääb S, Wilde AA, Schott JJ, Schulze-Bahr E, Bezzina CR.

			Analysis for Genetic Modifiers of Disease Severity in Patients With Long-QT Syndrome Type 2. Circ Cardiovasc Genet. 2015 Jun;8(3):447-56.
Professor Keith Channon		Identifying New Metabolic Mechanisms in Myocardial Infarction and Ischaemia-Reperfusion Injury In acute ST elevation myocardial infarction (STEMI), damage to the heart muscle is caused not only by ischemia due to the blocked coronary artery, but also by reperfusion injury when the artery is reopened at the time of emergency angioplasty (PCI). Reperfusion injury involves specific metabolic pathways in the mitochondria, recently identified by our collaborators (Ref 1). We will investigate these mechanisms in STEMI patients participating in the Oxford Acute Myocardial Infarction (OxAMI) study (e.g. Ref 2). We will use mass spectrometry metabolomic analyses of blood samples obtained from within the heart at the time of emergency PCI and relate these to other biomarkers and outcome measures. Understanding how these metabolic pathways are related to STEMI and reperfusion injury in humans may identify mechanisms that will be amenable to new therapies.	**Relevant publications:** 1. Ischaemic accumulation of succinate controls reperfusion injury through mitochondrial ROS. Chouchani ET, et al., Krieg T, Murphy MP. Nature. 2014;515:431-5. 2. Acute myocardial infarction activates distinct inflammation and proliferation pathways in circulating monocytes, prior to recruitment, and identified through conserved transcriptional responses in mice and humans. Ruparelia N et al., Channon KM, Choudhury RP. Eur Heart J. 2015 Aug 1;36:1923-34.
Professor Keith	Dr Mark Crabtree	Redox Regulation of Myocardial Mitochondrial Function by	1. McNeill E, Crabtree MJ, Sahgal N, Patel J, Chuaiphichai S, Iqbal AJ, Hale AB, Greaves DR, Channon KM. Regulation of iNOS function and cellular

Channon	Professor Barbara Casadei	Tetrahydrobiopterin in Heart Failure The essential cellular redox cofactor tetrahydrobiopterin (BH4) has important roles in nitric oxide synthesis, but we have recently discovered new requirements for BH4 in regulating cellular redox state that have potentially important implications for myocardial function and energy metabolism. We have created a cardiac-specific knockout mouse which is unable to synthesise BH4 in cardiac myocytes, resulting in profound cardiac BH4 deficiency. We will investigate how the requirement for BH4 alters heart function, and may predispose to heart failure through changes in cardiac metabolism and mitochondrial function.	redox state by macrophage Gch1 reveals specific requirements for tetrahydrobiopterin in NRF2 activation. *Free Radic Biol Med.* 2015;79:206-16. 2. Cardiomyocyte GTP cyclohydrolase 1 and tetrahydrobiopterin increase NOS1 activity and accelerate myocardial relaxation. Carnicer R, Hale AB, Suffredini S, Liu X, Reilly S, Zhang MH, Surdo NC, Bendall JK, Crabtree MJ, Lim GB, Alp NJ, Channon KM, Casadei B. *Circ Res.* 2012;111:718-27.
Professor Robin Choudhury		Effects of ischemic conditioning on exosome composition and monocyte function in acute myocardial infarction	Acute myocardial infarction activates distinct inflammation and proliferation pathways in circulating monocytes, prior to recruitment, and identified through conserved transcriptional responses in mice and humans. Ruparelia N, Godec J, Lee R, Chai JT, Dall'Armellina E, McAndrew D, Digby JE, Forfar JC, Prendergast BD, Kharbanda RK, Banning AP, Neubauer S, Lygate CA, Channon KM, Haining NW, Choudhury RP. Eur Heart J. 2015 Aug 1;36(29):1923-34. doi: 10.1093/eurheartj/ehv195. Epub 2015 May 16. PMID: 25982896
Professor Kieran Clarke		Dietary Ketones and Heart Failure	1. IUBMB Life, 51: 241–247, 2001 Ketone Bodies, Potential Therapeutic Uses; Richard L. Veech, Britton Chance, Yoshihiro Kashiwaya, Henry A. Lardy and George F. Cahill, Jr. 2. Neurobiol Aging. 2013;34:1530-1539. A ketone ester diet exhibits

			anxiolytic and cognition-sparing properties, and lessens amyloid and tau pathologies in a mouse model of Alzheimer's disease. Kashiwaya Y, Bergman C, Lee JH, Wan R, King MT, Mughal MR, Okun E, Clarke K, Mattson MP, Veech RL. 3. Regulatory Toxicology and Pharmacology 63 (2012) 401–408; Kinetics, safety and tolerability of (R)-3-hydroxybutyl (R)-3-hydroxybutyrate in healthy adult subjects; Kieran Clarke , Kirill Tchabanenko, Robert Pawlosky, Emma Carter, M. Todd King, Kathy Musa-Veloso, Manki Ho, Ashley Roberts, Jeremy Robertson, Theodore B. VanItallie, Richard L. Veech
Dr Matt Daniels	Dr Gil Bub (DPAG)	iPS modelling a novel human exercise induced arrhythmia syndrome with optogenetics, chemiluminescence and fluorescent optical mapping	1. Induced Pluripotent Stem Cell–Derived Cardiomyocytes - Boutique Science or Valuable Arrhythmia Model? Björn C. Knollmann; Circulation Research, 2013; 112: 969-976. Review. 2. Directed cardiomyocyte differentiation from human pluripotent stem cells by modulating Wnt/β-catenin signalling under fully defined conditions. Lian et al Nat Protoc. 2013, 8:162-75. 3. Recent progress in luminescent proteins development. Saito & Nagai Curr Opin Chem Biol. (2015);27:46-51. (review) 4. Optogenetic activation during detector "dead time" enables compatible real-time fluorescence imaging. Chang YF, Arai Y, Nagai T. Neurosci Res. 2012;73:341-7. 5. "Beauty is a light in the heart": the transformative potential of optogenetics for clinical applications in cardiovascular medicine. Boyle et al Trends Cardiovasc Med. 2015, 25:73-81. (review)
Dr Matt Daniels	Dr Daniel Ebner (TDI)	Drug screening of dynamic cellular processes in stem cell derived cardiomyocyte models of inherited human disease using high content imaging platforms and genetically encoded molecular sensors and actuators.	**1.** Gaudenz Danuser, Computer Vision in Cell Biology, Cell, 2011, Volume 147, Pages 973–978 (review) **2.** Sommer & Gerlich, Machine learning in cell biology – teaching computers to recognise phenotypes, J Cell Sci (2013) 126, 5529-5539. (review) **3.** Induced pluripotent stem cells as cardiac arrhythmic in vitro models and the impact for drug discovery, Šarić T et al Expert Opinion on Drug Discovery, (2014), 9, 55-76 (review) **4.** Cardiac optogenetics. Entcheva E. Am J Physiol Heart Circ Physiol. 2013;304:H1179-91. (review)

Professor Martin Farrall		Protein variant clustering in cardiovascular disease	1. Nature. 2015 Feb 5;518(7537):102-6. doi: 10.1038/nature13917. Epub 2014 Dec 10. Do R, Stitziel NO, Won HH, Jørgensen AB, Duga S, Angelica Merlini P, Kiezun A, Farrall M et al Exome sequencing identifies rare LDLR and APOA5 alleles conferring risk for myocardial infarction 2. BMC Bioinformatics. 2010 Jan 7;11:11. doi: 10.1186/1471-2105-11-11. Statistical method on nonrandom clustering with application to somatic mutations in cancer. Ye J1, Pavlicek A, Lunney EA, Rejto PA, Teng CH.
Professor Chris Garland		Endothelial cell control of arterial tone	1. EDHF: spreading the influence of the endothelium. Garland CJ, Hiley CR, Dora KA.Br J Pharmacol. 2011 Oct;164(3):839-52 2. Low intravascular pressure activates endothelial cell TRPV4 channels, local Ca2+ events, and IKCa channels, reducing arteriolar tone. Bagher P, Beleznai T, Kansui Y, Mitchell R, Garland CJ, Dora KA. Proc Natl Acad Sci USA. 2012 Oct 15.
Professor David R Greaves		Studying the role of macrophage metabolite receptors in diabetes and cardiovascular inflammation	1. Diet, metabolites, and "western-lifestyle" inflammatory diseases. Thorburn AN, Macia L, Mackay CR. 2. Immunity 2014; 40: 833-42. doi: 10.1016/j.immuni.2014.05.014. A Gpr120-selective agonist improves insulin resistance and chronic inflammation in obese mice. Oh da Y, et al. Nature Medicine 2014; 20: 942-7. doi: 10.1038/nm.3614.
Professor David R Greaves		What role do M2 polarised monocytes and macrophages play in arterial inflammation?	1. Macrophage differentiation and function in atherosclerosis: opportunities for therapeutic intervention? Williams HJ, Fisher EA, Greaves DR. J Innate Immun. 2012; 4: 498-508. doi: 10.1159/000336618. 2. Human CD68 promoter GFP transgenic mice allow analysis of monocyte to macrophage differentiation in vivo. Iqbal AJ, McNeill E, Kapellos TS, Regan-Komito D, Norman S, Burd S, Smart N, Machemer DE, Stylianou E, McShane H, Channon KM, Chawla A, Greaves DR.

			Blood. 2014; 124: e33-44. doi: 10.1182/blood-2014-04-568691.
Professor Paul Leeson		Targeting microvascular dysfunction to prevent hypertension in mother and offspring following	1. Lewandowski AJ, Davis EF, Yu G, Digby JE, Boardman H, Whitworth P, Singhal A, Lucas A, McCormick K, Shore AC, Leeson P. Elevated blood pressure in preterm-born offspring associates with a distinct antiangiogenic state and microvascular abnormalities in adults life. Hypertension 2015;65(3):607-14 2. Augustine D, Ayers LV, Lima E, Newton L, Lewandowski AJ, Davis EF, Ferry B, Leeson P. Dynamic release and clearance of circulating microparticles during cardiac stress. Circ Res 2014;114(1):109-1 3. Davis EF, Newton L, Lewandowski AJ, Lazdam M, Kelly BA, Kyriakou T, Leeson P. Pre-eclampsia and offspring cardiovascular health: mechanistic insights from experimental studies. Clin Sci 2012;123(2):53-72
Associate Professor Ming Lei		P21 activated kinase signalling in cardiac function, disease and therapy	1. Ke YB, Lei M, Collins TP, Rakovic S, Mattick P, Yamasaki M, Brodie MS, Terrar DA & Solaro RJ. Regulation of L-type calcium channel activity by P21 activated kinase-1 in guinea-pig sino-trial node pacemaker cells. Circ Res. 2007; 100: 1317-27. 2. Liu W, Zi M, Naumann R Ulm S, Jin J, Taglieri DM; Prehar S, Gui J, Tsui H, Xiao R, Neyses L, Solaro RJ, Ke Y, Cartwright EJ, Lei M & Wang X. Pak1 as a Novel Therapeutic Target for Anti-Hypertrophic Treatment in the Heart, Circulation. 2011;124:2702-15 3. Liu W, Zi M, Tsui H, Chowdhury SK, Zeef L, Meng Q, Travis M, Prehar S, Berry A, Hanley N, Neyses L, Xiao R, Oceandy D, Ke Y, Solaro RJ, Cartwright EJ, Lei M and Wang X. A novel immunomodulator, FTY-720 reverses existing cardiac hypertrophy and fibrosis from pressure overload by targeting NFAT signaling and periostin. Circulation Heart Fail. 2013; 6(4):833-44 4. Wang Y, Tsui H, Liu W, Shi Y, Wang R, Zhang Y, Solaro R, Ke Y, Zhang H, Cartwright E, Wang X and Lei M. P21 activated kinase-1 deficiency in cardiomyocytes increases in susceptibility to ventricular arrhythmogenesis in mice. Circulation: Arrhythm Electrophysiol 2014 (in press)

Associate Professor Mathilda Mommersteeg		Heart regeneration in a new, unique model: the Mexican cavefish	Kikuchi, K. & Poss, K. D. Cardiac Regenerative Capacity and Mechanisms. Annu. Rev. Cell Dev. Biol. 28, 719–741 (2012) Gross JB et al. The rise of Astyanax cavefish. Dev Dyn. 2015 Jan 20.
Professor Claudia Monaco	Ashok Handa	Single-cell profiling in vascular disease with mass cytometry	1. Bendall, S. C. et al. Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum. Science 332, 687-696, doi:10.1126/science.1198704 (2011). 2. Monaco C, Andreakos E, Kiriakidis S, Mauri C, Bicknell C, Foxwell B, Cheshire N, Paleolog E, Feldmann M. Canonical pathway of nuclear factor kappa b activation selectively regulates proinflammatory and prothrombotic responses in human atherosclerosis. Proc Natl Acad Sci U S A. 2004;101:5634-5639 3. Monaco C, Gregan SM, Navin TJ, Foxwell BM, Davies AH, Feldmann M. Toll-like receptor-2 mediates inflammation and matrix degradation in human atherosclerosis. Circulation. 2009;120:2462-2469
Professor Stefan Neubauer	Dr Craig Lygate	Assessing the therapeutic potential of augmenting cardiac energetics	1. Neubauer S. The failing heart--an engine out of fuel. New Engl J Med. 2007;356(11):1140-1151. 2. Lygate CA, Bohl S, ten Hove M, Faller KM, Ostrowski PJ, Zervou S, Medway DJ, Aksentijevic D, Sebag- Montefiore L, Wallis J, Clarke K, Watkins H, Schneider JE, Neubauer S (2012) Moderate elevation of intracellular creatine by targeting the creatine transporter protects mice from acute myocardial infarction. Cardiovascular Research 96:466-475 3. Lygate CA, Aksentijevic D, Dawson D, Ten Hove M, Phillips D, de Bono JP, Medway DJ, Sebag-Montefiore L, Hunyor I, Channon KM, Clarke K, Zervou S, Watkins H, Balaban RS, Neubauer S (2013) Living without creatine: unchanged exercise capacity and response to chronic myocardial infarction in creatine-deficient mice. Circulation Research 112:945-955
Professor Chris O'Callaghan		The macrophage response to atherogenic lipid.	1. Lipid-induced epigenomic changes in human macrophages identify a coronary artery disease associated variant that regulates PPAP2B expression through altered C/EBP-beta binding. Reschen ME, Gaulton KJ, Lin D, Soilleux EJ, Morris AJ, Smyth SS,

			O'Callaghan CA. PLOS Genetics. 2015 Apr 2;11(4):e1005061. 2. NF-kappa B regulates MICA transcription in endothelial cells through a genetically inhibitable control site. Lin D, Lavender H, Soilleux E, O'Callaghan CA. J Biol Chem. 2012 Feb 3;287(6):4299-310.
Professor David Paterson		Neural control and arrhythmia: electrophysiological, imaging and gene transfer strategy	1. Lu C-J, Hao, G. Nikiforova, N. Larsen, H.E., Liu, K., Cabtree, M.J., Li, D., Herring, H., & Paterson, D.J. (2015). CAPON modulates neuronal calcium handling and cardiac sympathetic neurotransmission during dysautonomia in hypertension. Hypertension 2015 Jun;65(6):1288-97 2. Li, D, Lu, C-J, Hao, G., Wright, H. Woodward, L, Liu, K., Vergari, E., Surdo, N.C., Herring, N., Zaccolo, M., & Paterson, D.J. (2015). Efficacy of B type natriuretic peptide is coupled to phosphodiesterase 2A in cardiac sympathetic neurons. Hypertension 2015 Jul;66(1):190-8
Professor David Paterson	Dr Neil Herring	The influence of neuropeptide Y on cardiac perfusion and arrhythmias	1. Shanks J, Herring N. (2013) Invited Review EB2012: Peripheral cardiac sympathetic hyperactivity: consequences in cardiovascular disease. Am J Physiol (DOI:10.1152/ajpregu.00118.2013) in press 2. Cuculi F, Herring N, De Caterina AR, Banning AP, Prendergast BD, Forfar JC, Choudhury RP, Channon KM, Kharbanda RK. (2013) Relationship of plasma Neuropeptide Y with angiographic, electrocardiographic and coronary physiology indices of reperfusion during ST elevation myocardial infarction. Heart 99(16), 1198-203 (See Editorial)
Professor Roger Patient		Cardiac regeneration in zebrafish	1. Curr Top Dev Biol. 2012 100:319-44. Cardiac regeneration. Choi WY, Poss KD. Nature. 2010 464: 606-9. Zebrafish heart regeneration occurs by cardiomyocyte dedifferentiation and 2. proliferation. Jopling C, Sleep E, Raya M, Martí M, Raya A, Izpisúa Belmonte JC. 3. Development. 2011 138: 3235-45. Fgf differentially controls cross-antagonism between cardiac and haemangioblast regulators. Simoes FC, Peterkin T, Patient R
Professor		Mammalian heart development and	1. Klotz, L., Norman, S., Vieira, J.M., Masters, M., Rohling, M., Dube, K.N.,

Paul Riley		regeneration	Bollini, S., Matsuzaki, F., Carr, C.A. & Riley, P.R. (2015). Cardiac lymphatics are heterogeneous in origin and respond to injury. Nature, 522, 62-67. 2. Petchey, L. K.*, Risebro, C. A.*, Vieira, J.M., Roberts, T., Bryson, J. B., Greensmith, L. Lythgoe, M. F. & Riley, P. R. (2014). Loss of Prox1 in striated muscle causes slow to fast skeletal muscle fibre-type conversion and dilated cardiomyopathy. PNAS 111, 9515-9520 3. Balmer*, G. M., Bollini*, S., Dubé, K. N., Martinez-Barbera, J-P, Williams, O & Riley, P. R. (2014). Dynamic haematopoietic cell contribution to the developing and adult epicardium. Nature Communications, DOI: 10.1038/ncomms5054. 4. Smart N, Bollini S, Dubé KN, Vieira JM, Zhou B, Davidson S, Yellon D, Riegler J, Price AN, Lythgoe MF, Pu WT, Riley PR. (2011), De novo cardiomyocytes from within the activated adult heart after injury. Nature.
Professor Peter Robbins		Non-invasive monitoring of cardiac output: Development of a new approach using in-airway molecular flow sensing	1. Thiele, R. H., Bartels, K., & Gan, T. J. (2015). Cardiac output monitoring: a contemporary assessment and review. Critical care medicine, 43(1), 177-185. 2. Cummings, B., Hamilton, M. L., Ciaffoni, L., Pragnell, T. R., Peverall, R., Ritchie, G. A., ... & Robbins, P. A. (2011). Laser-based absorption spectroscopy as a technique for rapid in-line analysis of respired gas concentrations of O_2 and CO_2. Journal of Applied Physiology, 111(1), 303-307.
Professor Jürgen Schneider	Dr Craig Lygate	Multi-parametric Magnetic Resonance Imaging of the Remodelling Mouse Heart	Magn Reson Med. 2012 Jan; 67(1):191-200. doi: 10.1002/mrm.22973 (2) Magnetic Resonance in Medicine 2013 70:1095–1105
Associate Professor Shankar Srinivas		Characterising the initiation of coordinated contractile activity in the embryonic heart	Chen, C-M., Miranda A. M. A., Bub, G., and Srinivas, S. (2015). Detecting cardiac contractile activity in the early mouse embryo using multiple modalities. Front. Physiol. 5:508. doi: 10.3389/fphys.2014.00508

Professor Rebecca Sitsapesan		Altered RyR2 function in inherited arrhythmic disorders and heart failure	1. O'Brien, F, Venturi E & Sitsapesan, R. (2015). The ryanodine receptor provides high throughput Ca^{2+}-release but is precisely regulated by networks of associated proteins: a focus on proteins relevant to phosphorylation. *Biochem Soc Trans.* 43(3):426-33. 2. Venturi, E., Galfré, E., O'Brien, F., Pitt, S.J., Bellamy, S., Sessions R.B. & Sitsapesan, R. (2014). FKBP12.6 activates RyR1: investigating the amino acid residues critical for channel modulation. *Biophys J.* 106, 824-33. 3. Galfré, E., Pitt, S. J., Venturi, E., Sitsapesan, M, Zaccai, N.R., Tsaneva-Atanasova, K., O'Neill, S. & Sitsapesan, R. (2012). FKBP12 activates the cardiac ryanodine receptor Ca^{2+}-release channel and is antagonised by FKBP12.6. *PLoS ONE*, 7, Issue 2, e31956. 4. (4) Carter, S., Pitt, S.J., Colyer, J. & Sitsapesan, R. (2011). Ca^{2+}-dependent phosphorylation of RyR2 can uncouple channel gating from direct cytosolic Ca^{2+}-regulation. *J. Membr. Biol.* **240**, 21-33.
Professor Rebecca Sitsapesan	Associate Professor Paolo Tammaro	Novel intracellular ion channels in the heart and their role in intracellular Ca^{2+}-release	1. Pitt, SJ, Lam, AKM, Rietdorf, K, Galione, A, and Sitsapesan, R (2014) Reconstituted Human TPC1 Is a Proton-Permeable Ion Channel and Is Activated by NAADP or Ca^{2+}. *Science Signal*, 7(326):ra46. 2. Pitt, SJ, Funnell, TM, Sitsapesan, M, Venturi, E, Rietdorf, K, Ruas, M, Ganesan, A, Gosain, R, Churchill, GC, Zhu, MX, Parrington, J, Galione, A, and Sitsapesan, R (2010) TPC2 is a novel NAADP-sensitive Ca^{2+} release channel, operating as a dual sensor of luminal pH and Ca^{2+}. *J Biol Chem*, 285(45):35039-46. 3. Venturi, E., Sitsapesan, R., Yamazaki, D. & Takeshima, H. (2013). TRIC channels supporting efficient Ca^{2+} release from intracellular stores. *Pflugers Arch-Eur. J. Physiol.* **465**, 187-195. 4. Yazawa, M., et al. (2007). TRIC channels are essential for Ca^{2+} handling in intracellular stores. *Nature* **448,** 78-82.
Dr Nicola		Approaches to enhance epicardial-based	1. Bollini S, Riley PR, Smart N. Thymosin β4: multiple functions in protection, repair and regeneration of the mammalian heart. Expert

Smart		regeneration and vascular protection	Opin Biol Ther. 2015 Jul;15 Suppl 1:163-74. 2. Smart N, Bollini S, Dubé KN, Vieira JM, Zhou B, Davidson S, Yellon D, Riegler J, Price AN, Lythgoe MF, Pu WT, Riley PR. De novo cardiomyocytes from within the activated adult heart after injury. Nature. 2011; 474 (7353):640-4. 3. Smart N, Risebro CA, Melville AA, Moses K, Schwartz RJ, Chien KR, Riley PR. Thymosin beta4 induces adult epicardial progenitor mobilization and neovascularization. Nature. 2007; 445 (7124):177-82 4. Rossdeutsch A, Smart N, Dubé KN, Turner M, Riley PR. (2012). Essential role for thymosin β4 in regulating vascular smooth muscle cell development and vessel wall stability. Circ Res. 111:e89-102.
Associate Professor Paolo Tammaro		Native and synthetic ion channels in the control of blood pressure	1. Smith KJ, Chadburn AJ, Adomaviciene A, Minoretti P, Vignali L, Emanuele E, Tammaro P. (2013) Coronary spasm and acute myocardial infarction due to a mutation (V734I) in the nucleotide binding domain 1 of ABCC9. Int J Cardiol. 168:3506-13. 2. Adomaviciene A, Smith KJ, Garnett H, Tammaro P. (2013) Putative pore-loops of TMEM16/anoctamin channels affect channel density in cell membranes. J Physiol. 591:3487-505.
Associate Professor Damian Tyler		Application of Hyperpolarized Magnetic Resonance Imaging for the Assessment of Treatment Response in the Diseased Heart	1. Hyperpolarized magnetic resonance: A novel technique for the in vivo assessment of cardiovascular disease. Circulation 124 (2011) 2. Role of pyruvate dehydrogenase inhibition in the development of hypertrophy in the hyperthyroid rat heart: A combined magnetic resonance imaging and hyperpolarized magnetic resonance spectroscopy study. Circulation 123 (2011)
Dr Ellie Tzima		How do vascular cells sense and respond to blood flow? An integrative approach to study	1. Collins C, Osborne LD, Guilluy C, Chen Z, O'Brien ET 3rd, Reader JS, Burridge K, Superfine R, Tzima E. Haemodynamic and extracellular matrix cues regulate the mechanical phenotype and stiffness of aortic endothelial cells. Nat Commun. 2014 Jun 11;5:3984

		mechanotransduction in cardiovascular disease.	2. Liu Y, Collins C, Kiosses WB, Murray AM, Joshi M, Shepherd TR, Fuentes EJ, Tzima E. A novel pathway spatiotemporally activates Rac1 and redox signaling in response to fluid shear stress. J Cell Biol. 2013 Jun 10;201(6):863-73.
Dr Ellie Tzima		Endothelial-cardiomyocyte communication in the heart; is it a two-way street?	1. McCormick ME, Collins C, Makarewich CA, Chen Z, Rojas M, Willis MS, Houser SR, Tzima E. Platelet endothelial cell adhesion molecule-1 mediates endothelial-cardiomyocyte communication and regulates cardiac function. J Am Heart Assoc. 2015 Jan 19;4(1):e001210. 2. McCormick ME, Rojas M, Moser-Katz T, Tzima E, Reader JS. Natural aminoacyl tRNA synthetase fragment enhances cardiac function after myocardial infarction. PLoS One. 2014 Oct 8;9(10):e109325.
Professor Hugh Watkins	Professor Charles Redwood and Dr Katja Gehmlich	Functional analyses of new disease genes for cardiomyopathy identified by whole genome sequencing	Watkins H, Ashrafian H, Redwood C. Inherited cardiomyopathies. N Engl J Med. 2011 Apr 28;364(17):1643-56. doi: 10.1056/NEJMra0902923.
Professor Manuela Zaccolo		Cyclic nucleotide microdomains and cardiac pathophysiology	1. Zaccolo M. Spatial control of cAMP signalling in health and disease. Curr Opin Pharmacol. 2011 Dec;11(6):649 55 2. Zoccarato A, Surdo NC, Aronsen JM, Fields LA, Mancuso L, Dodoni G, Stangherlin A, Livie C, Jiang H, Sin YY, Gesellchen F, Terrin A, Baillie GS, Nicklin SA, Graham D, Szabo-Fresnais N, Krall J, Vandeput F, Movsesian M, Furlan L, Corsetti V, Hamilton GM, Lefkimmiatis K, Sjaastad I, Zaccolo M. Cardiac Hypertrophy Is Inhibited by a Local Pool of cAMP Regulated by Phosphodiesterase 2. Circ Res. 2015 Aug 4. pii: CIRCRESAHA.114.305892. [Epub ahead of print] 3. Stangherlin A, Koschinski A, Terrin A, Zoccarato A, Jiang H, Fields LA, Zaccolo M. Analysis of compartmentalized

			cAMP: a method to compare signals from differently targeted FRET reporters. Methods Mol Biol. 2014;1071:59-71. doi: 10.1007/978-1-62703-622-1_5
Professor Manuela Zaccolo	Dr Konstantinos Lefkimmiatis	Mitochondrial cyclic AMP signalling in heart pathophysiology	1. Zaccolo M. Spatial control of cAMP signalling in heart and disease. Current Opinion in Pharmacology. 2011 Dec; 11(6):649-55 (http://www.ncbi.nlm.nih.gov/pubmed/22000603) 2. Lefkimmiatis K, et al. Store-operated cyclic AMP signalling mediated by STIM1. Nature Cell Biology. 2009 Apr; 11(4):433-42 (http://www.ncbi.nlm.nih.gov/pubmed/19287379) 3. Lefkimmiatis K, et al. The inner and outer compartments of mitochondria are sites of distinct cAMP/PKA signalling dynamics. Journal of Cell Biology. 2013 Aug; 5;202(3):453-62 (http://www.ncbi.nlm.nih.gov/pubmed/23897891)