



CARDIOVASCULAR DRUG DISCOVERY

WEDNESDAY 1ST NOVEMBER 2017

HOMERTON COLLEGE, HILLS ROAD, CAMBRIDGE CB2 8PH



Cambridge University Hospitals **NHS**
NHS Foundation Trust

Cambridge Biomedical Research Centre

NHS
National Institute for
Health Research

AstraZeneca 

 MedImmune

 GlaxoSmithKline

LEARNING OBJECTIVES

**UNDERSTANDING OF THE CHANGING LANDSCAPE OF DRUG DISCOVERY
PROCESS & CARDIOVASCULAR-SPECIFIC CHALLENGES**

**LEARNING EFFECTIVE WAYS TO OVERCOME BARRIERS TO DRUG DISCOVERY
RESEARCH**

**UNDERSTANDING OF HOW TO FORM & RUN ACADEMIC-INDUSTRIAL
COLLABORATIONS**

RESEARCH CASES

**Professor Margaret Ashcroft, Professor Richard Farndale,
Dr Stephanie Jung, Dr Thomas Krieg, Professor Nick Morrell,
Dr Andrew Murray, Dr Sanjay Sinha, Dr Takahiro Yamamoto**

INDUSTRY RESPONSES

**Dr David Budd (GSK), Dr Mark Bamford (GSK), Dr Nick Edmunds (AZ),
Dr Colin Fish (GSK), Dr Rajan Jethwa (Erudite Evolution),
Dr Jon Lyon (GSK), Mrs Su Moore (GSK)**

RESOURCES

[HTTP://WWW.EMI-TRAINING.ORG/](http://www.emi-training.org/)

ROYAL COLLEGE OF PHYSICIANS CPD

ACCREDITATION CODE: 113563 (7 POINTS)



SCHEDULE

FIRST SESSION – CASE STUDIES		LEARNING OUTCOMES
8.30-8.50am	Registration and Refreshments Alison Shrubsole Room	
8.50-9.00	Opening Remarks Dr Joseph Cheriyan	
9.00-9.30	“The path from first idea to a clinical study: challenges and principles” Dr Colin Fish (GSK)	Learn about drug discovery process and associated challenges – some specific to cardiovascular processes and others common to all drug discovery processes.
9.30-11.00	Three case studies followed by industrial responses and initial questions by delegates Case Study 1: Prof Nick Morrell “Targeting BMP2 for the treatment of pulmonary arterial hypertension” Response: Dr David Budd (GSK) Case Study 2: Prof Margaret Ashcroft & Dr Andrew Murray “Mitochondrial/CV toxicity/hypoxia” Response: Dr Jon Lyon (GSK) Case Study 3: Dr Takahiro Yamamoto “Cardiovascular toxicity” Response: Dr Nick Edmunds (AstraZeneca) “Physiologically-based PKPD models to predict drug-induced haemodynamic responses in health and disease”	CHAIR: Kevin O’Shaughnessy Audience participation and contribution to the discussion and debate is required in these sessions. Explore challenges and pitfalls in context with a specific case and real-time events.
11.00-11.30	Break	
11.30-1.00pm	Three case studies followed by industrial responses and initial questions by delegates Case Study 4: Prof Richard Farndale & Dr Stephanie Jung “Novel drug targets in AF/stroke” Response: Dr Mark Bamford (GSK) Case Study 5: Dr Thomas Krieg “Starting up a company” Response: Dr Rajan Jethwa (Erudite Evolution) Case Study 6: Dr Sanjay Sinha “Complex human models of disease to guide patient-specific therapies: Marfan syndrome as an exemplar” Response: Dr David Budd (GSK)	CHAIR: Dr Kevin O’Shaughnessy Audience participation and contribution to the discussion and debate is required in these sessions. Explore challenges and pitfalls in context with a specific case and real-time events.
1.00-2.00	Lunch	A chance to network and discuss the case studies further.

SECOND SESSION – CHALLENGE DISCUSSIONS

<p>2.00-3.00pm</p>	<p>Small group discussion about the challenges</p> <p>Led by the presenters of case studies and responses.</p>	<p>CHAIR: Dr Joseph Cheriyan</p> <p>Audience participation and contribution to the discussion and debate is required in these sessions.</p> <p>The aim is to identify possible ways to overcome presented challenges.</p>
<p>3.00-4.00</p>	<p>Panel discussion summarising ideas and follow-up steps for each case study</p> <p>Panel of Industry responders</p>	<p>Audience participation and contribution to the discussion and debate is beneficial in these sessions.</p> <p>The aim is to give each case study presenter concrete ideas for how to overcome the presented challenge.</p>
<p>4.00-4.15</p>	<p>Closing words</p> <p>Prof Nick Morrell</p>	<p>An opportunity to arrange private ‘surgeries’ for each case study.</p> <p>The presenters and industrial representatives to generate opportunities for collaborative research.</p>
<p>4.15-6.00</p>	<p>Networking and refreshments</p>	<p>Networking with colleagues from CATS, Entrepreneurs-in-Residence, Cambridge Enterprise, Milner Institute, Bayer, and local biotech.</p>
<p>6.00 6.30 7.00</p>	<p>Depart for Trinity Hall for dinner Drinks reception - Chetwode Room, Trinity Hall Dinner - Leslie Stephen Room, Trinity Hall</p>	<p>Dinner registrants only.</p>

SPEAKERS

<p>Dr Timothy Allsopp Entrepreneur-in-Residence, University of Cambridge</p>	
	<p>Tim has extensive industrial experience in commercial and clinical translation of stem cell science, extensive knowledge of the international cell therapies sector and product development experience from stints in both biotech and big pharma. As a company CSO he was instrumental in the growth from start up to public market listing of a pioneering stem cell biotech and he acts as subject matter specialist in evaluating technology for internationally funded, public sector and charity supported regenerative medicine programmes.</p>
<p>Professor Margaret Ashcroft Department of Medicine, University of Cambridge</p>	
	<p>The main goal of the Ashcroft laboratory is to understand the key cellular mechanisms involved in oxygen sensing and hypoxia signalling in mammalian cells. In particular, we have a strong interest in the hypoxia inducible factor (HIF) family of transcription factors and their role in cancer, renal disease and cardiovascular disease.</p>
<p>Dr Mark Bamford Discovery Partnership Leader, Discovery Partnerships with Academia (DPAc), GSK</p>	
	<p>Currently based in Stevenage, Mark Leads on DPAC. Previously held posts are Research Manager R&D, Senior Team Leader and Drug Discovery Project Leader, Medicinal Chemistry Team Leader and Drug Discoverer. Educated at University of Birmingham (1989).</p>
<p>Dr David Budd Director & Early Development Leader in the Pulmonary Vascular Injury group, part of the Respiratory Therapy Area, GSK</p>	
	<p>David Budd is based at the GSK Medicines Research Centre, Stevenage, UK and is involved in early discovery and development of new therapies to treat acute and chronic pulmonary vascular disorders with high unmet medical need, including Acute Respiratory Distress Syndrome (ARDS) and Pulmonary Arterial Hypertension (PAH).</p>
<p>Dr Joseph Cheriyan Consultant Physician, Director of Cardiovascular Trials Office & EMI Training Lead</p>	
	<p>Dr Cheriyan is a clinical researcher with interests in cardiovascular medicine particularly vascular function and inflammation. He is one of a few clinical triallists working on early phase experimental medicine studies of novel therapeutics, and has a unique post that combines close collaboration with industrial partners on the Addenbrooke's Biomedical Campus. His clinical service commitments are to the Department of Acute Medicine at Addenbrooke's Hospital. He is the Vice Chair of the local Research Ethics Committee, a member of the Management Board of the Cambridge Clinical Trials Unit and a Senior Physician and Clinical Pharmacologist to the GSK CUC in Cambridge.</p>
<p>Dr Nicholas Edmunds Head of New Modalities, Drug Safety and Metabolism, AstraZeneca</p>	
	<p>Following a PhD at the University of Bath and a 3 year post-doctoral research role at the University of Birmingham, Nick joined Pfizer, Sandwich UK, in 2002 working as a cardiovascular pharmacologist within the Cardiovascular Therapeutic Area. In 2008 he moved to Drug Safety as the Cardiovascular Discipline Leader. When the Sandwich UK site closed, he relocated to the Pfizer, Groton Connecticut to build a Cardiovascular Physiology group focussed on constructing disease-centric cardiovascular safety strategies within the Cardiovascular, Metabolic and Endocrine Research Unit. Nick joined AstraZeneca as Director of Safety Pharmacology in Drug Safety and Metabolism in 2014 based in Cambridge, UK. In 2016 Nick oversaw the creation of a new function within Drug Safety and Metabolism to provide focussed preclinical safety strategies for emerging nucleotide modalities, and he currently leads this effort as a Senior Director.</p>

Dr Richard Farndale

Professor of Matrix Biochemistry, University of Cambridge



My group has a long-standing interest in thrombus deposition on collagens of the blood vessel wall, mediated directly by platelet Glycoprotein VI (GPVI) and integrin $\alpha 2\beta 1$, and indirectly by von Willebrand factor/Glycoprotein Ib.

We work towards new drug targets for AF and stroke, and collaborate with Dr Sanjay Sinha (Medicine), Profs Ruth Cameron & Serena Best (Materials Science & Metallurgy), and Dr Thomas Krieg (EMIT) on the development of cardiac patches.

Dr Colin Fish

Vice President, WW NC SP, GSK



Colin Fish has worked in the pharmaceutical industry for more than 30 years (much of that at GSK), initially as a toxicologic pathologist, and subsequently serving on drug discovery and development project teams as the non-clinical safety team member. He now manages the group within GSK that assigns project team members in the disciplines of non-clinical safety and drug disposition to teams across all therapy areas, all modalities and all phases of development. He has extensive experience in helping teams to design integrated plans of non-clinical activities to support specific clinical plans and to meet regulatory expectations.

Dr Rajan Jethwa

Founder and CEO, Erudite Evolution



Dr Jethwa is a surgeon with extensive experience in C-level management, business strategy and transactions, focussed towards life sciences, healthcare, medical technology and pharmaceuticals. Dr Jethwa has a specific interest in venture capital and start up businesses, with experience of managing venture-backed start-ups. He has previously worked for Government, private equity, NHS Trusts, Primary Care Trusts and for multinational corporations advising on commercial strategies, transactions (buy side and sell side), market entry and product development.

Dr Stephanie Jung

Department of Biochemistry, University of Cambridge



Research Interests

Glycoprotein VI (GPVI) is a platelet-specific collagen receptor. When GPVI engages collagen, a signalling cascade is initiated, leading to platelet activation, aggregation, and thrombus formation. In the injured vasculature, hyperactive platelets bind to exposed subendothelial collagen, forming thrombi that can detach and occlude near or distal vessels resulting in ischaemic heart disease or stroke. Therefore, controlling the activity of GPVI offers a way to control thrombosis.

Dr Thomas Krieg

Lecturer in Clinical Pharmacology, University of Cambridge; Honorary Consultant Physician, Cambridge University Hospitals NHS Foundation Trust.



Research interests: MT ischaemic-reperfusion injury in MI & stroke.

Our research is directed toward identifying therapies that prevent cell death in ischaemic heart and the subsequent development of heart failure. In addition, we aim to develop treatment strategies targeting heart failure in disease models such as obesity, type 1 and type 2 diabetes, and ageing.

Dr Jon Lyon

Scientific Director and GSK Fellow



Jon has worked at GSK since 1997.

Currently Investigative Preclinical Toxicity & GSK Mitochondrial Network Lead, GSK, he has previously held roles as the manager of Molecular pathology and toxicology; an Investigator in Safety Assessment; an Investigator in Toxicogenomics.

Jon was also a post-doctoral research associate at the University of Glasgow (1995-97) and did his PhD at Imperial College (1995), London in Cell/Cellular and Molecular Biology; and a BSc at the University of Leicester (1991).

Professor Nick Morrell

BHF Professor of Cardiopulmonary Medicine, in the Department of Medicine, University of Cambridge, and Research Director of the National Pulmonary Hypertension Centre at Papworth Hospital



Nick Morrell is the BHF Professor of Cardiopulmonary Medicine, in the Department of Medicine, University of Cambridge, and Research Director of the National Pulmonary Hypertension Centre at Papworth Hospital. His laboratory is elucidating the genetic basis of pulmonary arterial hypertension (PAH), a rare disorder with a poor prognosis despite existing treatments. His research team seeks to exploit genetic findings to develop new therapies targeting the underlying molecular and cellular basis of PAH to identify disease-modifying approaches and improve clinical outcomes.

Dr Andrew Murray

University Senior Lecturer, Department of Physiology, Development and Neurosciences, University of Cambridge



Dr Andrew Murray studied Biochemistry at the University of Oxford, before continuing in the Department of Physiology, Anatomy and Genetics as a British Heart Foundation- supported DPhil student in the laboratory of Professor Kieran Clarke, studying the control of cardiac energy metabolism in heart failure and diabetes. Andrew continued in Oxford as a postdoctoral researcher, before moving to the University of Cambridge as a Research Councils UK Academic Fellow in 2007. Andrew is currently a University Senior Lecturer in the Department of Physiology, Development and Neuroscience. Andrew is a Principal Investigator at the Centre for Altitude, Space and Extreme Environment Medicine, and has taken part in several large-scale high altitude research expeditions including Caudwell Xtreme Everest in 2007 and Xtreme Everest 2 in 2013. As such, Andrew and his team have measured cardiac and skeletal muscle energetics in climbers returning from the summit of Everest and muscle mitochondrial function in Lowlanders and Sherpas at Mt Everest Base Camp. Andrew has published over 60 research papers to date, including articles in the *Lancet*, *Diabetes*, *Cell Metabolism*, *PNAS* and *Nature Cell Biology*. In 2010, he was invited by the Royal Society to represent the UK at the UK-Brazil Frontiers of Science symposium.

Dr Sanjay Sinha

British Heart Foundation Senior Research Fellow, in the Department of Medicine, University of Cambridge

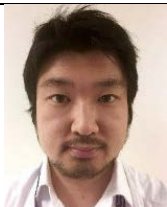


Dr Sinha's work is concerned with SMC development, lineage and disease; Modelling genetic diseases using patient-derived iPSCs; Myocardin as a key regulator of vascular disease.

His group's work combines the fields of stem cell biology and vascular biology to provide new insights into vascular smooth muscle cell development and novel treatments for vascular diseases. A major focus of the group is to use their established in vitro system and patient-derived iPS cells to model genetic disorders in which there is a key SMC phenotype. Marfan syndrome, in which aortic SMC loss and matrix breakdown lead to aortic dissection, is the exemplar for this approach.

Dr Takahiro Yamamoto

Clinical PhD Student, Experimental Medicine and Immunotherapeutics/AstraZeneca



Takahiro started his Clinical PhD with EMIT and Translational Safety at AstraZeneca in January 2016. He is a Clinical Pharmacology and Therapeutics trainee and was based at Guy's and St Thomas' Hospitals with the Clinical Toxicology department prior to commencing his studentship. His research interests include the cardiovascular effects of drugs and the current research project aims to generate unique human cardiovascular haemodynamic data that will be used to build quantitative PKPD systems models of the human cardiovascular system in health and disease.

USEFUL LINKS & CONTACTS

Cambridge Academy of Therapeutic Sciences (CATS)

<https://www.ats.cam.ac.uk>

Contact: Dr Paula Frampton, Executive Manager

Paula.Frampton@admin.cam.ac.uk

Cambridge Enterprise

<https://www.enterprise.cam.ac.uk>

Contact: Dr Amanda Wooding, Director

amanda.wooding@enterprise.cam.ac.uk

Milner Therapeutics Institute

<https://www.milner.cam.ac.uk>

Contact: Dr Kathryn Chapman, Executive Manager

k.chapman@milner.cam.ac.uk

Experimental Medicine Training Initiative

<https://emi.medschl.cam.ac.uk/>

Contact: Professor Ian Wilkinson, Director of OTR & EMI

ibw20@medschl.cam.ac.uk

Office for Translational Research (OTR)

<http://otr.medschl.cam.ac.uk/>

Contact: Dr Mellone Marchong, Translational Research Project Manager mm721@medschl.cam.ac.uk

Cambridge Cardiovascular

<https://www.cardiovascular.cam.ac.uk/>

Contact: Dr Katja Kivinen, Research Manager

kjk28@cam.ac.uk

Graduate & Clinical Academic Training

<https://gcat.medschl.cam.ac.uk/>

Contact: Elizabeth McIntyre, Graduate Programmes Manager

ejm45@medschl.cam.ac.uk

