



Experimental Medicine
Training Initiative

Renal Drug Discovery and Development

30TH MAY 2019

THE HOWARD BUILDING ASSEMBLY ROOM, DOWNING COLLEGE



Cambridge University Hospitals **NHS**
NHS Foundation Trust

Cambridge Biomedical Research Centre

NHS
National Institute for
Health Research

AstraZeneca 

 MedImmune

 **gsk**
GlaxoSmithKline

LEARNING OBJECTIVES

To understand renal drug discovery and development.

Understand the potential utility of CTLA-4 blockade in CKD.

Understand key elements of a clinical development plan for CKD.

Recognise the potential of an experimental medicine approach in phase 2 clinical development, through the example of a renal transplantation study.

Describe some of the potential challenges and limitations of an experimental medicine approach.

Understand how kidney organoid or 3-dimensional cultures that position renal cells on synthetic matrices can preserve in vivo tissue architecture and generate a tissue microenvironment for studying human disease.

Understand that models can overcome some of the logistical, ethical and scientific limitations of animal models or human clinical studies.

Recognise the involvement of the immune system, in particular T cells, as a driver of CKD progression; clinical development strategies for anti-inflammatory therapies for CKD.

SCHEDULE		SPEAKERS
09.00-9.30	Registration and Refreshments Drawing Room, Howard Building	
9.30-9.35	Welcome Howard Building Assembly Room	Dr Joseph Cheriyan & Dr Vik Selvarajah
9.35-10.05	Overview of drug development in Chronic Kidney Disease (CKD)	Dr Rona Smith Clinical Lecturer, University of Cambridge & Honorary NHS Consultant, Nephrology Cambridge University Hospitals Trust
10.05-10.35	Phase 3 trials – reasons for lack of success Webinar connection	Dr Phil Ambery Global Clinical Leader, Diabetes, AstraZeneca AB, Gothenburg
10.35-11.05	Pre-clinical development - Challenges in predicting human dose-response for CKD treatments	Dr Christine Ahlström, AstraZeneca Modelling & Simulation team leader, Gothenburg, AstraZeneca
11.05-11.20	BREAK – Drawing Room	
11.20-11.50	Recent developments in whole exome sequencing in CKD – potentials for future target identification 	Dr Slavé Petrovski Vice-president and Head of Genome Analytics for AstraZeneca Centre for Genomics Research (CGR), Cambridge
11.50-12.20	Research and advances on the treatment of Hyperkalemia	Dr Carol Moreno Senior Global Medical Affairs Lead, Astrazeneca Dr Toby Humphrey Clinical research fellow, department of medicine, University of Cambridge
12.20-13.30	LUNCH – Drawing Room	
13.30-14.00	Identifying therapeutic targets in immune-mediated kidney disease	Dr Menna Clatworthy Reader in Immunity and Inflammation, Department of Medicine, University of Cambridge, UK; Honorary Consultant Nephrologist, Cambridge University NHS Foundation Trust
14.00-14.30	T cell involvement in diabetic nephropathy & proteinuric renal disease: Abatacept (CTLA4-Ig) as a case study 	Dr Lutz Jermutus Senior Director, R&D, Product Development Team Leader Cardiovascular, Renal and Metabolism iMED, BioPharmaceuticals R&D, AstraZeneca. Industrial Fellow & Graduate Mentor Trinity Hall, University of Cambridge.
14.30-15.10	Break out groups CTLA-4: Re-purposing in CKD	Dr Victoria Parker Director of Clinical Development in CVRM (CV, renal and metabolism), AstraZeneca & Honorary consultant endocrinologist, Cambridge University Hospitals Trust
15.10-15.30	BREAK – Drawing Room	

15.30-16.00	Kidney organ culture models for studying human disease ★	Professor John Bradley Consultant Renal Physician and National Institute for Health Research Cambridge Biomedical Research Centre, and Director of Research for Cambridge University Health Partners
16.00-16.30	Belimumab – A phase 2 clinical trial in Renal Transplantation	Dr Shaun Flint Early Development Leader at GlaxoSmithKline and a physician with nephrology and vasculitis experience
16.30-17.00	Clinical Trials in Nephrology - Challenges and Opportunities.	Dr Thomas Hiemstra Honorary consultant nephrologist, Cambridge University Hospitals Trust & trials methodologist, Cambridge Clinical Trials Unit
17.00-17.10	Conclusion	Dr Joseph Cheriyan and Dr Viknesh Selvarajah
17.10- 19.00	Drinks reception & networking Drawing Room	
19.00	Dinner - The Maitland Room	

BIOGRAPHIES



Dr Phil Ambery

Global Clinical Leader, Diabetes, AstraZeneca AB, Gothenburg

Phil has considerable experience across all phases of clinical development in cardiovascular and metabolic diseases (CVMD) in the pharmaceutical industry. Having worked in medical affairs, late phase and early phase development for GSK from 2001-2014, he joined Medimmune where he was the lead member for the CVMD clinical group in Cambridge until 2018. He has now joined the late phase group for Cardiovascular, Renal and Metabolic diseases (CVRM) in Sweden for AZ where he is a global clinical leader. He has a particular interest in incretins for the treatment of Type 2 diabetes and in Type 1 diabetes immune modulation. He is a specialist

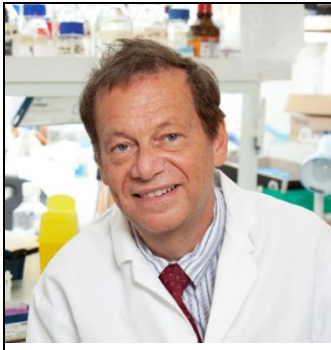
partner for the General Medical Council in academic or research certification, taking a particular interest in the licensing of doctors via the academic route, and still practises as an Acute Medicine Physician in Addenbrookes.



Dr Christine Ahlström

Modelling & Simulation team leader, Gothenburg, AstraZeneca

Christine Ahlström is a biotechnical engineer by training and holds a PhD in Pharmacology from University of Gothenburg with focus on mathematical modelling of adaptation in drug response. Dr Ahlström joined AstraZeneca in 2011 as a pharmacokinetic and pharmacodynamic scientist within the cardiovascular, renal and metabolism area and is now leading the Modelling & Simulation team within this unit at AstraZeneca in Gothenburg. She has over the last five years primarily focused on the treatment of chronic kidney disease (CKD) with translation of dose-response from animal to human as expertise area and has supported numerous drug project within the CKD space with quantitative and translational aspects.



Professor John Bradley

Consultant Renal Physician and National Institute for Health Research Cambridge Biomedical Research Centre, and Director of Research for Cambridge University Health Partners

John Bradley is a consultant physician and Director of the National Institute for Health Research Cambridge Biomedical Research Centre, and Director of Research for Cambridge University Health Partners. He completed undergraduate medical training in

Nottingham and trained in renal medicine in Cambridge, before undertaking research fellowships at Harvard, Yale and Cambridge Universities. As a NIHR Senior Investigator his research focuses on TNF signalling in the microvasculature. He was made a Commander of the Order of the British Empire in the Queen's birthday honours in 2015.



Dr Joseph Cheriyan

Consultant Physician & Clinical Pharmacologist at Addenbrooke's Hospital, Associate Lecturer, University of Cambridge, Director of the Cardiovascular Trials Office, Vice Chair of the Cambridge Research Ethics Committee, EMI Training Lead

Joseph is an active clinical researcher with interests in cardiovascular medicine particularly vascular function and inflammation and is uniquely the only MHRA accredited Phase I/II clinical triallist on the Cambridge Biomedical Campus working on early phase

experimental medicine studies since 2006. His post combines NHS research within a University Department, in close collaboration with GSK's only remaining in house Clinical Unit, where he is seconded as a Senior Clinical Pharmacologist.



Dr Menna Clatworthy

Reader in Immunity and Inflammation, Department of Medicine, University of Cambridge, UK; Honorary Consultant Nephrologist, Cambridge University NHS Foundation Trust; Fellow and Director of Studies (Clinical Medicine), Pembroke College, Cambridge; Director, NIH-OxCam PhD Scholars Programme

Dr Clatworthy took up a University Lecturer post in Cambridge in 2012, established her own lab in 2013 and was awarded a Readership and tenure in 2017. She is a clinician

scientist and divides her time between clinical work as a nephrologist, managing kidney and kidney-pancreas transplant recipients, and research. Her lab is focused on understanding the regulation of antibody generation and effector function, novel methods of targeting humoral immunity in kidney transplantation and investigating how the kidney microenvironment shapes local immune responses. This work ranges from experimental medicine studies in patients, in collaboration with industry partners, through to basic immunology studies, using murine models. The lab has a strong emphasis on integrating the use of primary human tissues into all of their studies, ensuring translational relevance, including collaborations with colleagues at the Wellcome Sanger Institute utilising single cell technologies to understand tissue-resident immune cells.



Dr Shaun Flint

Early Development Leader at GlaxoSmithKline and a physician with nephrology and vasculitis experience

Shaun Flint is an Early Development Leader at GlaxoSmithKline and physician with nephrology and vasculitis background. He has worked in early phase R&D within industry for the last 3 years, where his current role involves leading a cross-functional team developing a novel asset in Ph2. Prior to that, he completed a translational medicine PhD at Cambridge University and specialist training in renal medicine in Australia.



Dr Thomas Hiemstra

Honorary consultant nephrologist, Cambridge University Hospitals Trust & trials methodologist, Cambridge Clinical Trials Unit.

Dr Thomas Hiemstra is an honorary consultant nephrologist at Addenbrooke's Hospital. He is a trials methodologist with the Cambridge Clinical Trials Unit, where his primary focus is on efficient trials design. He leads a portfolio of trials in nephrology and related disciplines and serves on several trials steering committees and data monitoring committees. He chairs the UK Kidney Research Consortium Renal Trials Network (UKRTN), is president elect of the International Clinical Trials Centre Network (ICN) and leads the International Society of

Nephrology Trials Toolkit working group.

Dr Toby Humphrey

Clinical research fellow, Department of Medicine, University of Cambridge; Honorary Specialty Registrar in Nephrology and General Medicine, Cambridge University Hospitals NHS Foundation Trust.

Dr Toby Humphrey is a Clinical Research Fellow supported by the Experimental Medicine Training Initiative in the Department of Medicine at the University of Cambridge. His PhD is focussed on novel approaches to the emergency management of hyperkalaemia with an interest in the design of interventional trials in this area. Prior to this he completed an undergraduate degree in Molecular Biology from Durham University before studying medicine in Nottingham. His clinical training has been spread across London and the East of England. He continues to work as a Nephrology Registrar in Cambridge.



Dr Lutz Jermutus PhD FRSC FFPM (Hons)

Senior Director, R&D, Product Development Team Leader Cardiovascular, Renal and Metabolism iMED, BioPharmaceuticals R&D, AstraZeneca. Industrial Fellow & Graduate Mentor Trinity Hall University of Cambridge

Lutz Jermutus is Product Development Team Leader and Senior Director, R&D, in the cardiovascular, metabolic and renal diseases unit of AstraZeneca. He is responsible for leading novel candidate drugs to clinical proof-of-concept including MEDI0382, a GLP-1/Glucagon dual peptide agonist for the treatment of Type 2 Diabetes.



Dr Carol Moreno

Senior Global Medical Affairs Lead, - Cardiovascular, Renal and Metabolic- AstraZeneca

Carol Moreno Quinn is the Sr. Global Medical Affairs Lead for Lokelma in CVRM (CV, renal and metabolism) at AstraZeneca, since 2018. Prior to this she was a principal scientist in MedImmune, where she lead the CKD research group since 2014.

Carol obtained her MD and PhD in Physiology and Pharmacology in Murcia (Spain) and, after a postdoctoral fellowship in genomics, developed her research and academic

career at the Medical College of Wisconsin, where she served as faculty until 2013. She has published over 50 manuscripts on renal and cardiovascular disease.



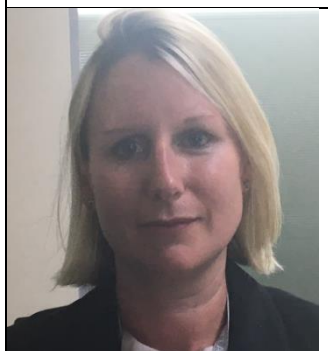
Dr Slavé Petrovski

Vice-president and Head of Genome Analytics for AstraZeneca Centre for Genomics Research (CGR), Cambridge

Slavé is a human & statistical geneticist by training with over 10 years' experience leading large-scale human genomics studies and in this time has contributed to shaping the field of contemporary population and statistical genomics.

At AstraZeneca, Slavé leads the CGR Genome Analytics and Informatics (A&I) organisation where he's responsible for architecting and driving the company's Genomics Initiative A&I strategies. He has built in-house expertise across five key

domains: Informatics Systems Design & Development, Robust Bioinformatic Pipelines, Statistical Genetics, Innovative Methods Development, and Applied Genome Analytics to large-scale cohorts, including studies of over 3,000 individuals with Chronic Kidney Disease (CKD).



Dr Victoria Parker

Director of Clinical Development in CVRM (CV, renal and metabolism), AstraZeneca & Honorary consultant endocrinologist, Cambridge University Hospitals Trust.

Victoria Parker is a Director of Clinical Development in CVRM (CV, renal and metabolism) at AstraZeneca and an Honorary Consultant Endocrinologist at CUH. She joined industry just under 3 years ago and prior to this undertook her clinical training at CUH and her PhD at the Institute of Metabolic Science, University of Cambridge.



Dr Viknesh Selvarajah

Clinical Lecturer in Clinical Pharmacology & Therapeutics, Division of Experimental Medicine and Immunotherapeutics, University of Cambridge

Co-organiser of the EMI Renal Drug Development event 2019, Viknesh initially trained in Scotland and subsequently completed his specialist training in Clinical Pharmacology and Nephrology in Cambridge as well as a PhD in 2018.

Dr Rona Smith

Clinical Lecturer, University of Cambridge & Honorary NHS Consultant, Nephrology Cambridge University Hospitals Trust.

Rona is a clinical lecturer in experimental medicine and nephrology with a particular interest in vasculitis and autoimmunity and the use of biologics in treatment strategies in this area.



Professor Ian Wilkinson

Professor of Therapeutics, Director of Cambridge Clinical Trials' Unit, Director of the Office of Translational Research, University of Cambridge, Director of the Experimental Medicine Training Initiative

Ian has a long track record in clinical pharmacology and arterial haemodynamics. His research interest is in clinical/experimental studies designed to understand the mechanisms underlying arteriosclerosis and cardiovascular disease, and to understand the importance of novel biomarkers of arterial function in risk prediction. He directs the Cambridge Clinical Trials' Unit and is also a director of the Office of Translational Research in Cambridge and the Experimental Medicine Initiative. He has considerable experience of translational research, and in forming academic collaborations with Industry.

BACKGROUND READING

★ Al-Lamki RS, Bradley JR, Pober JS. Human Organ Culture: Updating the Approach to Bridge the Gap from In Vitro to In Vivo in Inflammation, Cancer, and Stem Cell Biology. *Front Med (Lausanne)*. 2017; 4: 148.

★★ Inhibition of T-cell activation by the CTLA4-Fc Abatacept is sufficient to ameliorate proteinuric kidney disease
<https://www.physiology.org/doi/pdf/10.1152/ajprenal.00179.2016>

★★★ Diagnostic Utility of Exome Sequencing for Kidney Disease
Emily E. Groopman, Maddalena Marasa, Sophia Cameron-Christie, Slavé Petrovski, Vimla S. Aggarwal, Hila Milo-Rasouly, Yifu Li, Junying Zhang, Jordan Nestor, Priya Krithivasan, M Wan Yee Lam, Adele Mitrotti, et al.
<https://www.nejm.org/doi/10.1056/NEJMoa1806891>

RESOURCES

<http://www.emi-training.org/>

Royal College of Physicians CPD 124778 accreditation under application