COMPARE

Newsletter **Edition 2,** December 2016

Welcome

University of Birmingham
David Hodson, Steve Thomas, Steve Briddon and Natalie Poulter have been formally appointed as COMPARE PIs.
University of Nottingham
Sally Utton, Programme Operations Manager, and Chris McGrath have joined the Nottingham COMPARE office. Sally will be working in both Nottingham (Mon/Tue/Fri) and Birmingham (Wed/Thur).
Recruitment—Birmingham
Administrator—Interviews 11th January 2017
Image Analyst—Closing date 14th December 2016
Microscope Officer— closing date 14th December 2016

Houses of Parliament Reception

Houses of Parliament

On the 22nd November, Birmingham and Nottingham Universities hosted a reception at the Houses of Parliament, in conjunction with the East and West Midlands All Party Parliamentary Group to celebrate five years of partnership between the leading institutions in the West and East Midlands. What makes the Birmingham-Nottingham partnership distinctive is the depth of commitment and scope for staff to work together. This includes education, learning, teaching, and professional services, as well as a sustained approach to research collaborations. The partnership is unique in scale and depth and we have built trust and momentum, leading to a £10m investment over the next 5 years. The reception aimed to celebrate and promote the collaboration, in particular:

- To raise the profile of the partnership at a national level and celebrate its successes.
- **To publicise the launch of COMPARE.**
- To highlight the range of collaborative work that has been undertaken.
- To explain how our bilateral collaboration contributes to the broader Midlands agenda.
- To discuss how regional collaborations such as ours have a part to play in post-Brexit Britain.

Key Dates

COMPARE Launch
29th June 2017
Birmingham

Strategic Oversight Group (SOG)
19th December (UoN)

29th March (UOB)

26th June (UoN)

International Advisory Board (IAB)
28th September 2017 (EMCC)

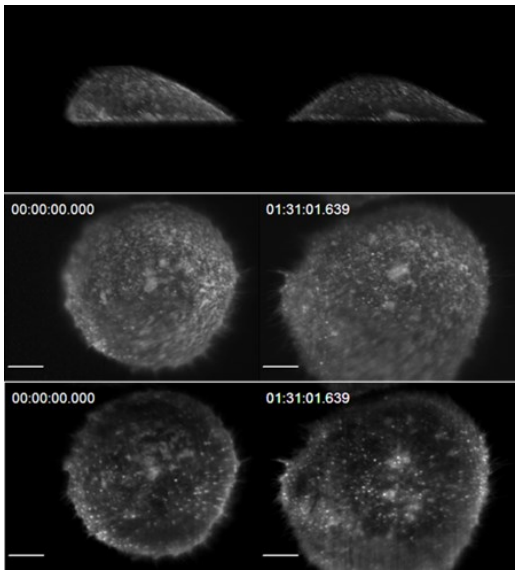
COMPARE Away Day
29th September
EMCC

Management Board
10th February 2017 (UoN)

PostDoc/PhD Away Day
Summer 2017 (tbc)

RESEARCH SPOTLIGHT—Malou Zuidscherwoude

The **Lattice LightSheet** is an advanced light sheet microscope invented by Nobel Laureate Eric Betzig. This system creates an exceptionally thin light sheet, which allows for superior optical sectioning and minimal background caused by out of focus light. Compared to other microscopy techniques, cells can be imaged with high signal to noise with relative low doses of light. This attribute makes this system very suitable for sensitive cells or for 3D experiments with a duration of hours to days, as there is limited photo-toxicity. Moreover, the sensitive and fast camera allows for acquisition of 3D stacks at high speed. Currently we are using the Lattice LightSheet to visualize plasma membrane receptors dynamics and their internalisation in 4D.



Bone marrow derived megakaryocytes from LifeAct-GFP mice were allowed to spread on fibrinogen coated coverslips. Stacks were taken every minute for over 2 hours, with minimal photo bleaching and no apparent cell stress. The first time point (left) and the spreading cell after one and a half hour imaging (right) are shown. The panels show a side view (top; maximum intensity projection of 3D volume), top view (middle; maximum intensity projection) and the coverslip contact side, showing individual actin structures including podosomes (bottom panel; single plane). Scale bars represent 10µm

Successful External Grant Applications

£1.5m Joint Wellcome Investigator Grant, Steve Watson (PI) and Robert Ariens (Leeds); Jonas Emsley (UoN). Match funding for diSPIM microscope

€1.7m ERC Start Up Grant, David Hodson (PI): match funding for two photon microscope

Please forward details of all grant submissions and outcomes to Sally Utton.

Medication under the spotlight—David Hodson

Many diseases rely upon medication for their treatment or cure. Yet, modern day drug therapy continues to be based upon 20th century principles. We get ill, we take a pill and then attempt to go about our daily lives, sometimes suffering from unpleasant side effects. On the flip side, a large number of potentially life-saving treatments never get to market, or are removed from sale, because of their questionable safety profiles.

Read the full article; http://www.birmingham.ac.uk/research/perspective/medication-under-the-spotlight.aspx

Successful COMPARE Funding Applications

Title	Applicants	Award (£)
Quantifying CLEC-2 clustering by Fluorescence Fluctuation Microscopy techniques.	Steve Watson (UoB); Steve Briddon (UoN)	£5,200
Elucidating Activin A/Receptor Complex Trafficking and Signalling: Link to Cell Differentiation	Carol Murphy, Steve Thomas (UoB)	£25,000
Covalent labels for the super-resolution high-affinity tracking of a class B GPCR	David Hodson (UoB), David Calebiro (Würzburg), Johnsson/Broichhagen (MPI Heidelberg)	£42,983
Shedding of N-cadherin by Tspan15/ADAM10 complexes: development of fluorescence correlation spectroscopy (FCS) to image shedding in real-time	Steve Briddon (UoN), Nick Holliday (UoN) Mike Tomlinson (UoB), Steve Hill (UoN)	£3,600
Investigating platelet collagen receptor GPVI shedding by TspanC8/ADAM10 complexes	Natalie Poulter (UoB), Steve Watson (UOB), Mike Tomlinson (UoB), Tim Self (UoN)	£48,537
Developing GPR126 ligands to probe GPR126 function in the lung	IP Hall, P Fischer, I Sayers, B Kellam (UoN)	£48,704
COMPARE Molecular Probe Provision; Research to Commercialisation	Barrie Kellam, Steve Hill (UoN)	£49,393
Platelet membrane receptor glycoprotein Ib (GP)Ib-IX complex analysed using super-resolution light microscopy	Jonas Emsley (UoN), Natalie Poulter (UoB), Tim Self (UoN)	£50,000
An investigation of the link between actin dynamics and the oligomerisation of membrane proteins	Robert Neely, Iain Styles, Steve Thomas, Natalie Poulter and Steve Briddon	£50,000
Development of an imaging apparatus, compatible with parallel haemodynamic measurement technologies, for the in vivo assessment of allosterism and biased signalling from GPCRs and VEGFR2.	Jeanette Woolard & Steve Hill (UoN)	£40,000

Birmingham Medical School

Refurbishment

Birmingham

New labs and office space in Birmingham are well underway and are on target to open at the end of January 2017

Nottingham

Nottingham are currently identifying a new laboratory and office space for Senior Fellows, Chair and admin team, along with microscopes and analysis station. Completion April/May 2017

Branding and Communications

A COMPARE logo has been drafted and is awaiting approval by both Universities.

Once agreed, the logo should be used on every talk that originated from COMPARE funding and should acknowledge the funding source.

A branding and communications policy is in draft at present and will be circulated to all once it is finalised.

Team Science

Natalie Poulter has requested information on key interests, skills and animal models held by each group within COMPARE. Please return your forms as soon as possible to Chris McGrath, so that the data can be collated and circulated accordingly. This is also the opportunity to provide contact details for Postdoc and PhD students to facilitate organisation of an Away Day 2017.

Launch Event—watch this space!

Discussions are underway for a Nobel Prize winner to give the Keynote speech at the Compare Launch on the 29th June 2017. More news to follow.

Distribution Lists

We are currently compiling email distribution lists which we will be able to share in due course. Please keep us informed of new staff and leavers, so we can keep these up to date.

Contact Us

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Meeting Membership

International Advisory Board

Chair	Patrick Vallance	GlaxoSmithKline
Deputy	Steve Rees	AstraZeneca
Members	Nigel Bunnett	Columbia University Medical Centre
	Kurt Ballmer-Hofer	University of Basel
	Kathleen Caron	University of North Carolina
	Anne Ridley	Kings College London
	Evi Kostenis	University of Bonn
	Jason Swedlow	Dundee University
	Victor Tybulewicz	The Crick Institute

Strategic Oversight Group

Jessica Corner	PVC, Research and Knowledge Exchange, UoN
John Atherton	PVC Faculty of Medicine and Health Sciences, UoN
Tim Softley	PVC for Research and Knowledge Transfer, UoB
David Adams	PVC, Head of College of Medical and Dental Services, UoB
Steve Hill	Co-Director, COMPARE, UoN
Steve Watson	Co-Director, COMPARE, UoB
Rebecca Lewis	UoN/UoB Collaboration Manager
Sally Utton	Programme Operations Manager

Management Board

UoN	**UoB**
Steve Hill (Chair)	Steve Watson (Chair)
Jeanette Woolard (Deputy Director)	Iain Styles (Deputy Director)
Steve Briddon (Academic Lead)	Steve Thomas (Academic Lead)
David Bates (PI)	Roy Bicknell (PI)
Ian Hall (PI)	Carol Murphy (PI)
Peter Fischer (PI)	Natalie Poulter (PI)
Sally Utton	Rob Neely (PI)
	Rebecca Lewis

International Advisory Board Members

Chair – Patrick Vallance
Job title: President, Pharmaceuticals R&D
Institution: GlaxoSmithKline

Patrick was appointed President, Pharmaceuticals R&D AT GSK, in January 2012. Prior to his appointment he was Senior Vice President, Medicines Discovery and Development. He is a member of the Corporate Executive Team. Patrick joined the Company in May 2006 as Head of Drug Discovery.

Prior to joining GSK Patrick was a clinical academic and led the Division of Medicine at University College London. He has over 20 years' experience of research clinical medicine, general internal medicine, cardiovascular medicine and clinical pharmacology. He was elected to the Academy of Medical Sciences in 1999.
Patrick has been on the Board of the UK Office for Strategic Co-ordination of Health Research (OSCHR) since 2009.

Deputy Chair: Steve Rees
Job title: Vice President of Screening and Sample Management
Institution: AstraZeneca

Steve Rees is currently Vice-President of Screening Sciences and Sample Management at AstraZeneca with global responsibility for High Throughput Screening, Compound Management, the human tissue BioBank and the provision of SAR biology support to preclinical discovery projects.

Prior to joining AstraZeneca, Steve worked at GlaxoSmithKline for 24 years in various roles including that of Director of the Screening and Compound Profiling Department at GlaxoSmithKline in Stevenage. Steve has been responsible for developing hit identification, compound profiling and compound management strategies for AstraZenenca and previously GlaxoSmithKline. Steve has led multiple international collaborations and has sponsored the development and implementation of a range of cellular assay technologies for ion channel, GPCR and other target classes.

Steve has been Chair of the Europe Council of SLAS since 2013 and Section President for the Society for Laboratory Automation and Screening (2011) and a Board member of European Laboratory Robiotics Interest Group (ELRIG) (2013).

Member: Kathleen Caron
Job title: Professor and Chair of Department of Cell Biology & Physiology
Institution: University of North Carolina, Chapel Hill

Kathleen completed her undergraduate degrees in biology and philosophy at Emory University in Atlanta, she completed her graduate degree at Duke University, in Durham, N.C.

Kathleen's current studies make use of in vitro cell culture approaches and sophisticated genetic mouse models to further elucidate the function of AM and its receptors in the growth and function of the lymphatic vasculature. Since the AM receptor is one of the first identified GPCRs involved in lymphangiogenesis13, we are interested in developing and launching a high throughput, small molecule interrogator screen aimed at identifying compounds that selectively target the AM receptor for modulation of lymphatic endothelial cell growth and permeability. Eventually, we hope to use AMtargeted therapies in preclinical animal tumour models for the inhibition of tumour lymphangiogenesis and distal metastasis.

International Advisory Board Members

Member: Anne Ridley
Job title: Professor of Cell Biology
Institution: Kings College London

Anne joined Kings College in 2007 as Professor of Cell Biology. Prior to joining Kings Anne was Professor of Cell Biology (2003) and Group Leader of the Ludwig Institute of Cancer Research (1993-2007) at University College London. Anne completed her PhD in Biology at the University of London in 1989 and postdoctoral research at the Whitehead Institute (MIT) and the Institute of Cancer Research UCL.

The Ridley group are investigating the mechanisms of cell migration, focusing on the roles of Rho GTPases and the cytoskeleton. Cell movement is driven by the cytoskeleton, principally by filaments made of actin molecules. Cells need to move during embryonic development to form tissues such as the brain and heart. In adults, cells also move in order to repair and replace damaged tissues, and to fight infections. For example, during infections leukocytes in the bloodstream have to cross blood vessel walls to get into the tissues. We study how leukocytes adhere to and migrate across endothelial cells, which line blood vessels. Cell migration also contributes to the development of human diseases, including cancer and heart disease. Cancer cells in tumours often become motile, invade surrounding tissues, and eventually spread to other sites in the body via the bloodstream. We are studying the intracellular signalling pathways regulating each step of this process of cancer metastasis. We use a wide variety of techniques in our research, including time-lapse and confocal microscopy, molecular biology, biochemistry and cell biology. A major emphasis of our current research is to use RNAi to identify novel proteins involved in cancer cell migration and invasion.

Member: Evi Kostenis
Job title: Professor, Department Chair, Director of Institute
Institution: University of Bonn

Research focus

G protein-coupled receptors (GPCRs), G proteins, GPCR-mediated signal transduction

Technologies / resources

Cell culture, molecular biology, Transgenic mouse models, Bioluminescence Energy Transfer (BRET), Fluorescence Energy Transfer (FRET), Resonant waveguide grating Biosensor measuring station (Corning ® Epic ®), High throughput screening in recombinant and primary cells by Corning ® Epic ® technology

Member: Nigel Bunnett
Job title: Professor of Surgery
Institution: Columbia University Medical Centre

Nigel joined the Department of Surgery and Pharmacology at Columbia University in 2016. Prior to joining Columbia Nigel was at Monash University, Melbourne (2011) as NHMRC Australia Fellow, Professor of Pharmacology and Medicine, and Deputy Director of the Monash Institute of Pharmaceutical Science and the University of California, San Francisco (1987), where he became Professor of Surgery and Physiology, Vice Chair of Surgery, and Director of the UCSF Centre for the Neurobiology of Digestive Diseases.

Nigel's research focuses on two families of proteins at the surface of nerve cells that control pain, itch and inflammation: G protein-coupled receptors and transient receptor potential ion channels. G protein-coupled receptors are the largest class of signalling proteins, participate in all physiological and patho-physiological processes, and are the target of one third of clinically used drugs. The small family of transient receptor potential ion channels also control important biological processes and are an emerging therapeutic target. G protein-coupled receptors and transient receptor potential ion channels allow nerves to sense noxious, irritating and inflammatory stimuli. Their activation leads to the sensations of pain and itch, and controls the process of inflammation.

International Advisory Board Members

Member: Jason Swedlow
Job title: Professor of Quantitative Cell Biology
Institution: Dundee University

In 1998, Jason established his own laboratory at the Wellcome Trust Biocentre, University of Dundee, Scotland as a Principal Investigator and Wellcome Trust Career Development Fellow. He was awarded a Wellcome Trust Senior Fellowship in 2002, and named Professor of Quantitative Cell Biology in 2007.

Jason earned a BA in Chemistry from Brandeis University in 1982. He obtained his PhD in Biophysics with Profs D. A. Agard and J. W. Sedat, finishing in 1994. Jason was a postdoctoral fellow at UCSF and then Harvard Medical School from 1994 and 1998, supported by a Damon Runyon Walter Winchell Cancer Research Fund Fellowship from 1995 to 1997.

Jason's lab focuses on studies of mitotic and interphase chromosome structure and dynamics.
Jason is the Co-Director of the Analytical and Quantitative Microscopy Course and
Co-founder of The Open Microscopy Environment (OME), along with Peter Sorger and Ilya Goldberg.

Member: Victor Tybulewicz
Job title: Head of Division of Immune Cell Biology
Institution: The Francis Crick Institute

Victor is a Group Leader and Head of Division of Immune Cell Biology at the Francis Crick Institute. He obtained his BSc from Imperial College London and then studied for a PhD at the MRC Laboratory of Molecular Biology in Cambridge, under the supervision of Dr John Walker, working on the ATP synthases of bacteria and mitochondria. As a postdoctoral fellow at the Whitehead Institute, Massachusetts Institute of Technology, under the supervision of Professor Richard Mulligan, he worked on methods to target mouse embryonic stem cells.

Ii 1991 Victor set up a group at NIMR using mouse genetics to study signal transduction in lymphocytes, exploring the roles of signalling molecules such as Syk, Vav1, Rac1 and Rac2 in B and T cell development, activation and survival. In addition, with Elizabeth Fisher of UCL he used his knowledge of genetic manipulation of mice to generate a novel model of Down Syndrome, the Tc1 mouse strain. This strain of mice carries a freely segregating copy of human chromosome 21 (Hsa21). Analysis of the mice showed that they have a series of phenotypes resembling the human condition, including defects in learning and memory, cardiac and craniofacial defects, and altered megakaryopoiesis.

Currently Victor and Elizabeth Fisher are generating a large panel of mice trisomic for different sets of Hsa21 genes or their mouse orthologues, and using these to identify 'dosage-sensitive' genes that are required in three copies to cause specific Down syndrome phenotypes.

Member: Kurt Ballmer-Hofer
Job title: Group Leader
Institution: Universitat Basel

Kurt's research focuses on the analysis of cellular signalling pathways which are fundamental to modern biology and are required for understanding cellular processes in organ homeostasis and in disease. Insight into the combined behaviour of the plethora of diverse, interacting cellular signalling molecules can be achieved through adequate integration of experimental, mathematical and computational sciences.

Recent technical advances in genomics, proteomics, and metabolomics have radically transformed our approach to understanding cellular signalling networks in biology and will be instrumental in dissecting their roles in the development of disease. Our experimental approach is to identify the molecular components of cellular signalling systems and their interactions, to monitor the effect of perturbations on the performance of these components and to build mathematical models that allow predictions of system behaviour.